IN ENGLISH TRANSLATION

ON TO FURTHER ACHIEVEMENTS IN CHEMICAL SCIENCE AND INDUSTRY.

The Soviet people meet the thirty-fifth anniversary of the Great October Socialist Revolution with new victories, and with new and magnificent achievements on the road to communism.

The recently concluded XIXth Congress of the Communist Party of the Soviet Union summarized the results of these victories, and projected a majestic perspective of the building of a communist society.

In the directives of the XIXth Party Congress, in conformance with the Five-Year-Plan, the basic economic principle of socialism has found its bright reflection in the straightforward and scientifically-sound treatise by Comrade Stalin, "Economic Problems of Socialism in the U.S.S.R." The essential characteristics and demands of this principle are: "provision and guarantee of maximum satisfaction for the constantly growing material and cultural demands of the whole society, by way of continuous growth and improvement of socialist production, based upon superior technical arts". [1]

The brilliant composition of Comrade Stalin, "Economic Problems of Socialism in the U.S.S.R.", ideologically arms the party and the Soviet people, and defines the scientific bases for development of socialist economy, and indicates the course of gradual transition from socialism to communism.

For the new five-year period, the projected industrial productivity increase for 1955, as against 1950, is approximately 70%. Together with the enormous growth in industrial, agricultural and consumer goods production, the directives project vigorous progress in all branches of the national economy, considerable increase in national revenue for the U.S.S.R., further elevation of the standard of living and of the cultural level of the Soviet people.

Soviet science in our socialist fatherland has reached unprecedented range and flourish.

If bourgeois science has now rolled down into a bog of reaction, and if it now serves American imperialism in the realization of its predatory plans, then our science is the science of creation, it serves the interests of the nation, and is directed toward the solution of the most important problems of the national economy and culture.

The significance of science in the life of our society increases more and more.

The Party and the Government have built and equipped an enormous network of scientific research institutes, among which are many chemical institutes.

For the scientists, congenial conditions have been created for fruitful creative work, and extensive training of scientific cadre has been provided for.

The number of scientific research institutes, laboratories and other scientific institutions has increased from 1560 in 1939 to 2900 at the beginning of this year. Within the same period, the number of scientific workers has almost doubled. During the past five-year period, the expenditure by the state for the needs of science has amounted to 47.2 billion rubles.

The Academy of Sciences of the U.S.S.R. has become the very world center of science. Under the guidance of the state, the Academy and its scientific establishments have grown to unprecedented, verily gigantic, sizes: The Academy budget, in comparison with prerevolution, has increased almost 700 times, and the number of scientific workers — 60 times. The number of books and journals published by the Academy has also increased almost 25 times. Such a tempo of development of science was never dreamed of, and now cannot be dreamed of by scientists of the capitalist countries. The bourgeois governments, first of all the U.S.A. magnates, do not begrudge the means for that aspect of science which serves for the enslavement and extermination of nations, which justifies and proclaims the cannibalistic plans of its masters.

Our Soviet science will grow and develop further. The Congress directives stipulate: "To expand, during the five-year period to come, the training of scientific and scientific-pedagogical teams, through post-graduate fellowships to the universities and scientific-research institutes, to approximately twice that of the preceding five-year plan.

"To facilitate the work of the scientific-research institutes and the scientific work of the universities, the scientific facilities are to be more amply utilized for solution of the more important problems of development of the national economy,of the general conclusions of advanced tests, experiments to secure wide practical application of scientific discoveries. To cooperate in every way with scholars, to strengthen the bond between science and production in working out theoretical problems in all fields of knowledge" [2].

The party, the government, and Comrade Stalin, personally, have always paid close attention to the chemical industry, to chemical science, and to the training of highly qualified teams of chemists. In Tsarist Russia, the chemical industry was in a state of incubation. Beyond doubt in that time we had some most prominent scholars, among the outstanding chemists of which were, for example, N. N. Zinin, A. M. Butlerov, D. I. Mendeleev, and many others, who enriched not only Russian, but also world knowledge with most important discoveries, but their theoretical investigations and discoveries did not, and could not, find, appropriate practical application in Russia.

Inexhaustible riches lay beneath Russian soil, uninvestigated, unutilized, while chemical products were imported. Only during Soviet rule has domestic chemistry developed and grown stronger. This growth has become singularly noticeable during the years of the Stalin   five-year plans. In 1933, Comrade Stalin had already said: "We did not have any major and modern chemical industry. We have it now" [3].

In 1934 the XVII Congress   of the All-Union Communist Party (Bolsheviks) — the convention of the victors — resolved: "To achieve definite improvements in the development of the chemical industry, securing broad chemicalization of all branches of the national economy, and the defensability of the country." [4].

As this resolution was fulfilled during the second five-year plan there were great achievements in the chemical industry, particularly in the petroleum, coal, and oil-shale industries, in ferrous and non-ferrous metallurgy, in fertilizers, in the nitrogen industry, in synthetic rubber, plastics and synthetic fibers. In the third five-year plan — the five-year plan of chemistry, and in the fourth — the postwar five-year plan, chemical industry and science achieved even greater and more outstanding successes. Thus, in the fourth five-year plan, i.e., toward the end of 1950, the chemical industry exceeded prewar production by 1.8 times, in the nitrogen fertilizers — by 2.2 times, in the potassium fertilizers — by 1.4 times, and in the phosphate — by 1.9 times. The prewar level of production was exceeded also in other aspects of the chemical industry — in soda, synthetic rubber, plastics and others.

Soviet chemical science has always helped industry actively and efficiently. The success in the petroleum industry, where, through the combined efforts of scholars, geologists and chemists, many new oil fields were discovered and exploited, serves as a striking example. Even more impressive is the example of the exceptionally important work of S. V. Lebedev. His most valuable theoretical investigations form the foundation for the vigorous growth and development of the synthetic rubber industry, so much needed for our national economy. There is no greater happiness for the scholar than to see how his investigations are being rapidly realized for the benefit of his native land.

S. V. Lebedev has said with satisfaction: "The government has decided to convert the success attained by me and my coworkers into the basis for constructing a new branch of industry..... There is not the slightest doubt that only with us, in the comty of the building of socialism, is such a great creative range possible. The greatest happiness is to see one's thought converted into a deed of such grandeur."

The directives from the XIXth Congress   of the Communist Party of the Soviet Union, for the fifth five-year plan of development for the U.S.S.R. for 1951-1955, projects further the rise of the chemical industry. The more important productivities will increase toward 1955, as compared with 1950, approximately in the following ranges: rubber — by 82%, soda ash — by 84%, caustic soda — by 79%, mineral fertilizers — 88%.

To the scholars and workers in the chemical industry, the XIXth Congress   has assigned the task of development, in every way possible, of synthetic rubber production on the basis of petroleum gas utilization, of increase in production of plastics, dyes, raw materials for artificial silk, development of production of synthetic materials — substitutes for the non-ferrous metals. The Congress   directives also stipulate increased production outputs for ammonia, sulfuric acid, synthetic rubber, synthetic alcohol, soda, mineral fertilizers, particularly in the granular form, and chemical control agents to combat agricultural plant pests.

Also contemplated is the systematic construction   of mineral fertilizer factories, thus securing the indispensable mineral ferilizer production developments for the years to follow. The Congress directives demand a wide incorporation of oxygen into the technological processes of ferrous and non-ferrous metallurgy, into gas production from coals, into the celluloid and the cement industries.

There is no doubt that Soviet chemists will fulfill, with honor, the tasks designed for the five-year plan by the directives. The sum totals of 1951, and the agricultural achievements of the present year, demonstrate that the Soviet people have already achieved considerable success in the fulfillment of the tasks presented by the five-year plan. The chemical industry is now endowed with excellent techniques, has qualified cadres, and the enterprises are not experiencing raw material shortages. The fact is that shortcomings in the work should be decisively removed by means of an extensive development of socialist competition, which will increase productivity, by observing strict economy, finding new reserves. We must develop a creative union between knowledge and practice—the foundations for any scientific and technical progress. Experience has shown that where such accord is established science itself also flourishes, and procures help for the practical workers through better and more rapid solution of production problems.

For the fulfillment of the five-year plan, science has been assigned an active role.

Scientists are responsible for achieving complete utilization of the fuel resources —coal, peat and oil-shales, in the capacity of raw chemical materials. Such raw materials should be burned only after extraction of gas, tar and other substances. Scientists should realize in full the D. I. Mendeleev concept about the complete chemical utilization of petroleum as a raw material, from which we can obtain alcohols, synthetic rubber, dyes and many other materials essential for our national economy. Industry has set before the chemist one more very important problem— the creation of exceptionally durable plastics, which are extra-hard and extra-stable to chemical reactions, and which possess fixed properties which would enable them to replace the valuable metals.

Comrade G. M. Malenkov, in a report of the Party Central Committee for the XIXth Congress, has pointed out a series of shortcomings and distortions which were disclosed by the Central Committee of the All- Union Communist Party (Bolsheviks) in the various departments of science. He pointed out that "in various branches of science there is still incomplete liquidation of monopoly by separate groups of scholars, who brush off new manpower developments, fencing themselves off from criticism, and attempt to solve scientific problems by administrative means. No single branch of science can successfully develop in a stuffy atmosphere of mutual eulogy and overlooking of errors; attempts to affirm the monopoly of separate groups of scholars inevitably engenders stagnation and decay in science" [5].

Every scholar should remember these words, and should answer the call of the Congress "to promote further the advancement of Soviet science, with the aim of attaining first place in world science" [6].

Gigantic, noble, and not an easy aim! But it is within the power of Soviet scientists. Already, various branches of our science have left behind scientists of the capitalist countries. We must surpass them in all branches of science, and we will!

Soviet scientists, armed with the all-triumphant teaching of Marxism-Leninism, inspired by the resolutions of the XIXth Congress of our party, and the speech of our leader, under the guidance of the Communist Party, together with the great coryphaeus of science, Iosif Vissarionivich Stalin, will be in the first ranks of the builders of communism, and the champions of peace throughout all the world.

LITERATURE CITED

[1] I. Stalin. "Economic Problems of Socialism in the U.S.S.R.". State Political Press, 1952, page 40.

[2] Pravda, October 12, 1952

[3] I. Stalin. Problems of Leninism, page 373.

[4] All-Union Communist Party (bolsheviks) in the resolutions and decisions of the conventions, conferences and plenum of the Central Committee, Part II, page 572.

[5] G. Malenkov. Report to the XIXth Congress of the Party, Concerning the Work of the Central Committee of the All-Union Communist Party (Bolsheviks). State Political Press, 1952, page 96.

[6] Ibid, page 78.
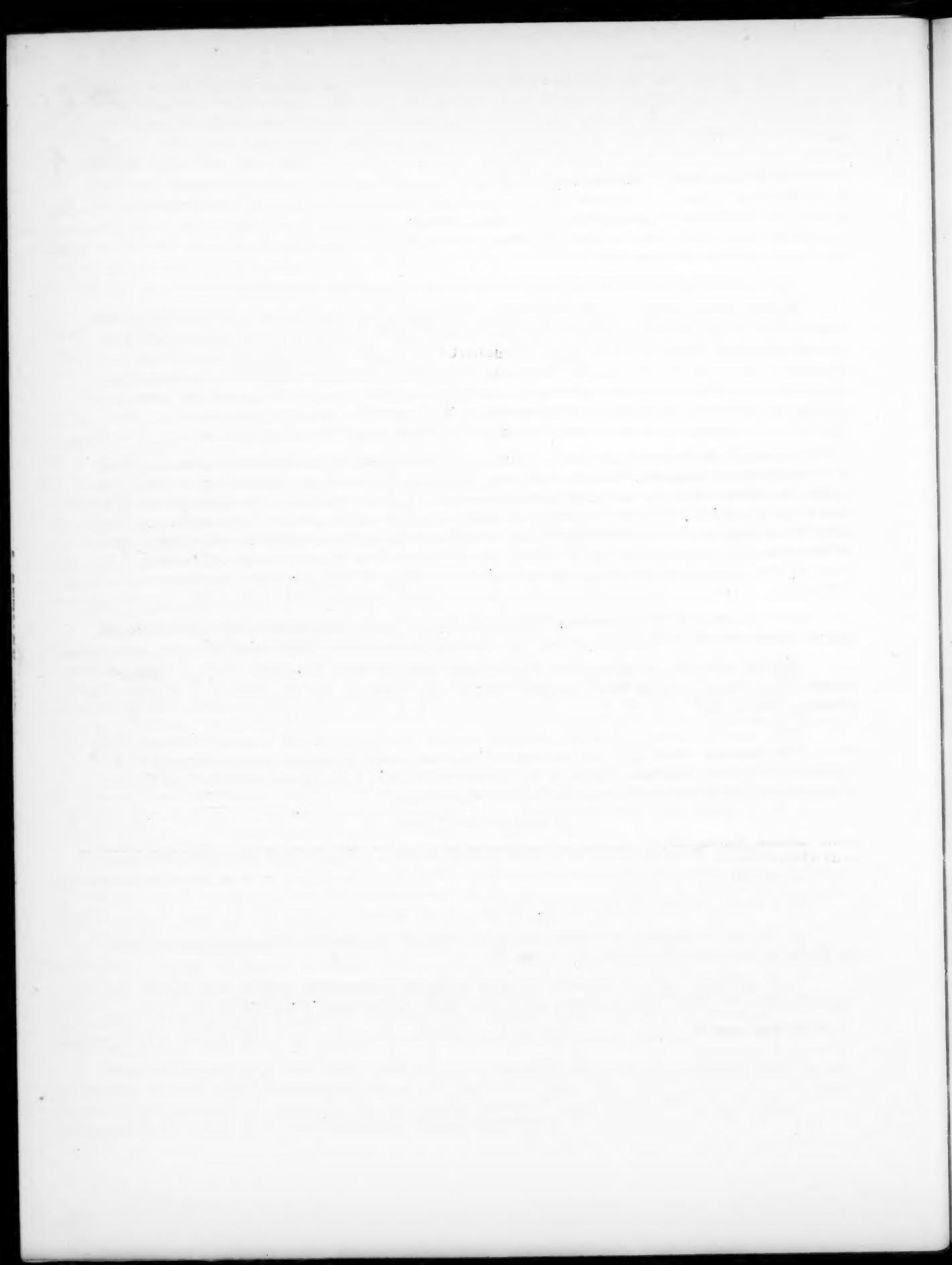
SOME PHYSICO-CHEMICAL PROPERTIES OF ARSENOUS ACID ANHYDRIDE

V. M. Borisov and M. G. Gorshtein

Up to the present time, many physico-chemical properties of arsenous acid anhydride have not been precisely determined, nor are there any consistent data concerning the same. Questions of the structures of the various forms of arsenous acid anhydride relate particularly to such properties as melting point, stabilities of its various forms, and others.

The existence of three solid forms of arsenous anhydride is known: two crystalline — octahedral and monoclinic, and one amorphous — vitreous. The data of Smith and Beljars [1], concerning their discovery of three new forms of arsenous acid anhydride, were not confirmed upon examination. As was determined [2], the octahedral form of arsenous acid anhydride, to which is usually ascribed the formula, As_2O_3, gives a molecular lattice composed of molecules of As_4O_6 (Figure 1, a). The arrangement of the individual molecules in the crystal is similar to that of the carbon atoms in diamond (Fig. 1, b).


Fig. 1. Arsenous Acid Anhydride.
a - molecule of As_4O_6 in the octahedral modification of the crystal; b - arrangement of As_4O_6 molecules in the octahedral modification of the crystal. 1 - arsenic atoms, 2 - oxygen atoms

The arsenic and oxygen atoms within the molecules are saturated by their own primary valences, while the bonding between the molecules in the lattice is realized by auxiliary valences.

Because the arsenous acid anhydride, in its gaseous state at 800°, forms two-dimensional molecules of As_4O_6, the breaking of only two auxiliary bonds is required for transition of the octahedral form of arsenous acid anhydride into the gaseous state.

The structural monoclinic form of arsenous acid anhydride has not been determined up to the present time, on which matter there is only a series of assumptions. Of these, the best, explaining the properties of arsenous acid anhydride monoclinic structure, is the one presented in Fig. 2 [3]. The composite parts of the lattice, in this case, are bound together by primary valences.

On the average, the transition of the monoclinic form of arsenous acid anhydride to the vapor state requires the rupture of two primary valences; because of further evolution of energy upon saturation of the liberated valences, the activation energy should decrease at the same time: this is confirmed by the smaller heat of sublimation of the monoclinic form, as compared with that of the octahedral.

In view of the fact that the glassy form of arsenous acid anhydride converts readily into the octahedral form, even under normal conditions, some authors make assumptions about the close relationship between the glassy and the octahedral structural forms.

Such an inference appears to be incorrect for two reasons. 1) The glassy form of arsenous acid anhydride transforms readily into the octahedral only under defined conditions, namely, when sufficiently pulverized, and when in the presence of moisture. The authors verified, experimentally, that the glassy arsenous acid anhydride, in various fragment sizes, transformed only partially into the octahedral form, at the surface, after preservation under normal conditions for one year. The basic mass of both the large and the small fragments remained in the glassy form.

2) The sublimation of the vitreous (or glassy) form is considerably smaller than that of the octahedral,
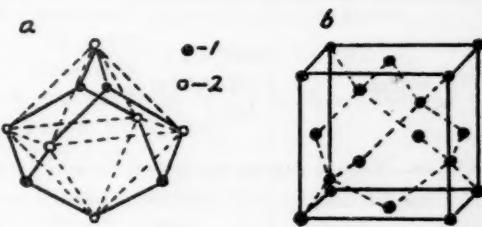
and, as is known, for the vaporization or volatilization processes of various forms of one and the same substance, that form has the greatest volatilization rate whose structure in the solid form is identical with, or has the greatest similarity to, the structure in the gaseous form.

On the basis of investigation presented [3], it can be assumed, through the process of "compulsory condensation" of arsenous acid anhydride, that the glassy structural form of arsenous acid anhydride may be represented by an irregular, repetitive atomic lattice.
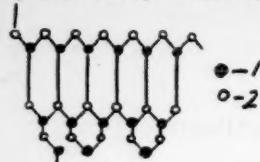
Fig. 2. Monoclinic structural modification of arsenous acid anhydride.
1 - arsenic atoms, 2 - oxygen atoms

Data on conditions for the stability of the various forms of solid arsenous acid anhydride, and the melting point of the octahedral form are inconsistent, as can be seen from the table.

These inconsistencies are explained by the fact that the determinations were carried out by different procedures and mainly by indirect methods (by vapor tension, solubility in alkali and in acid, and so forth).

The authors have carried out investigation of transition of the octahedral form of arsenous acid anhydride to the monoclinic, and verification of the melting point for the octahedral form by a direct method involving the use of thermal analysis.

Sub- ject mat- ter No.	Author	Ref. Lit. No.	Year	Transition temp. of octahedral form into the mono- clinic (°C)	Melting Point (°C) of the form	
					Octa- hedral	Mono- clinic
1	Welch and Daschak	4	1915	100	251	315
2	Raschton and Daniels	5	1926	100	275	313
3	Smith and Beljars	1	1933	200	—	—
4	Schulman and Schumb	6	1943	–13	—	—

The octahedral form of arsenous acid anhydride, which was obtained by recrystallization from hydrochloric acid as a condensate from a Schumb special sublimator, was heated a sealed glass tube in a 40 g weighed portion. The content of As_4O_6 in the arsenous acid anhydride used for the heating, was 99.98%. The homogeneity and identity of these samples with that of the octahedral form were verified by microscopic examination.

None of the thermodiagrams taken show the presence of any transition points from arsenous acid anhydride octahedral form to the monoclinic in the range up to the melting point of the octahedral form.

As can be seen from the thermodiagrams (Figures 3 and 3a) the octahedral form starts to melt at 270°.

Before melting starts, an exothermal effect takes place (ascending curve) at the expense of internal structure transformation of the substance.

From the thermodiagrams it also follows that the melting point of the octahedral form is polythermal, since melting starts at 270° and is fully terminated at 290-295°.

As is known, arsenous acid anhydride upon heating melts to a viscous mass, which, under the influence of its own weight, slowly changes form. Even at the boiling point, the viscosity of this mass is so great that threads from the viscous mass do not collect into drops.

It can be assumed that, at the start of the melting, there are formed infinite chains of arsenous acid anhydride (As_2O_3) compounds, and that upon further heating there occurs a definite correlation between the finite tetrahedral molecules of the arsenous acid anhydride octahedral form, and the infinite chains being formed at the melting, depending upon the rate of heating, analogous to the correlation between ring structure, S_8, in rhombic sulfur and the infinite chains in plastic sulfur. This evidently gives the polythermal melting temperature of the arsenous acid anhydride octahedral form.

The transition heat for the octahedral to monoclinic form is comparatively small (6100 cal/mole). It is possible that this effect may not be detectable on the thermograms. But the complete melting of the arsenous acid anhydride samples at the melting temperature of the monoclinic form, and the absence of a second melting point on the thermograms, confirm the failure to form noticeable quantities of the monoclinic form when the octahedral form is heated to its melting temperatures.

Figs. 3 and 3a, Thermograms of arsenous acid anhydride fusibility.

Thus, it can be considered that the stable form of arsenous acid anhydride is the octahedral form, up to the points of melting.

SUMMARY

1. The question of the structures of the various forms of arsenous acid anhydride has been defined more accurately, on the analytical basis of the available data on the physico-chemical properties of arsenous acid anhydride.

2. It was ascertained that the melting temperature of arsenous acid anhydride octahedral form is polythermal. Crystals of the octahedral form of arsenous acid anhydride start to melt at 270°C. Complete fusion is effected at 290-295°.

3. The stable form of arsenous acid anhydride is the octahedral, up to the melting temperatures.

LITERATURE CITED

[1] A. Smith and Beljars, Z. Phys. Chem., A — 61, 287 (1933).

[2] Ya. K. Syrkin and M. E. Dyatkina. The Chemical Bond and the Structure of Molecules. Sci. Tech. Institute (1946).

[3] S. Stranski and G. Wolff, Z. Elektrochem. and Z. ang. Phys. Chem., B — 53, 1 (1950).

[4] Welch, Duschak, Bur. Min., 81, 15 (1919).

[5] E. Ruschton and Daniels, J. Am. Chem. Soc., 48, 2 (1926).

[6] G. Schulman and Schumb, J. Am. Chem. Soc. 65, 872 (1943).

INTERACTION OF METALLIC BERYLLIUM WITH SOLID CRYSTALLOHYDRATES

O. P. Alekseeva

In 1905 Mikhailenko demonstrated that when magnesium powder and solid crystallohydrates are mixed, hydrogen is evolved. Together with Mushinsky, he has investigated fifty-three various crystallohydrates, during which in only three cases was hydrogen not evolved.

In 1940, Semishin, proceeding from the assumption that hydrogen evolution during magnesium interaction with solid crystallohydrates is the result of $H^{\cdot}$ ion reduction by magnesium atoms, and that not only magnesium, but every other metal, whose reduction potential $(nEMe/Me^{\cdot\cdot})$ is greater than that of the potential H_2 gas/2$H^{\cdot}$, should undergo analogous reaction, decided to investigate the interaction of aluminum and of zinc with solid crystallohydrates. He investigated the interaction of aluminum with forty two, and of zinc with forty three crystallohydrates. With aluminum, the evolution of hydrogen was not observed in eight cases and with zinc in three cases.

As with the reaction with magnesium, the nature of the crystallohydrates influences the intensity of reaction with aluminum and zinc, the greatest activity being possessed by crystallohydrate salts of hydrochloric acid, whereas the presence of $SO_4^{\cdot\cdot}$ in the crystallohydrate lowers considerably its activity toward the metal.

A comparison of data from the works of Mikhailenko and Semishin indicates that aluminum is less reactive toward the water of crystallohydrates in comparison with that of magnesium and that zinc has even less reactivity.

These metals can be arranged in the sequence: Mg-Al-Zn, as regards their activity toward the water of the solid crystallohydrates.

Since the reduction potential of beryllium exceeds, considerably, the potential of H_2 gas/2$H^{\cdot}$, it could be expected, on the basis of the works mentioned, that beryllium should displace hydrogen from the water of the solid crystallohydrates, according to the scheme:

$$Be + 2H^{\cdot} \longrightarrow H_2 + Be^{\cdot\cdot},$$

on initial reaction, according to Semishin:

$$Be + 2[Me(H_2O)_{n-1}(OH)^{\cdot}]^{+m-1} + 2H^{\cdot} \longrightarrow Be^{\cdot\cdot} + 2[Me(H_2O)_{n-1}(OH)^{\cdot}]^{+m-1} + H_2 \uparrow .$$

EXPERIMENTAL

In order to conduct the experiments, the authors used a compact lump of beryllium, with a beryllium content of 99.5%, which was available in the laboratory. From the lump were hammered off small fragments; the fragments were finely powdered in a mortar, the fine powder was always sifted through the same sieve, and was preserved in a ground glass stoppered bottle. In the course of the work, it was noticed that freshly-prepared beryllium powder was considerably more active than the powder preserved for several days, after which beryllium powder preserved for twenty-four hours was used in all experiments. The crystallohydrate salts used for the experiments were analytically pure. The salt was ground in a mortar to the finest powder, and a maximum of 0.01 mole was placed in a 50 ml flat-bottomed flask. Into the same flask was placed a weighed quantity of beryllium powder. In order to obtain comparative results, calculation of the weight of crystallohydrate and of metal was made according to the reaction:

$$Be + 2HOH^{\cdot} = Be(OH)_2 + H_2.$$

The flask was stoppered with a cork having a tube leading to the gasometer. A one-liter Erlenmeyer flask served for the gasometer. The gas volume was determined by measuring the volume of water which flowed out of the gasometer under the pressure of evolving gas. The flask contents, after stoppering with the cork, were thoroughly mixed by shaking the flask. In those cases where reaction began immediately upon contact of crystallohydrate with metal powder, the latter was not sprinkled into the flask, but was placed in the inclined neck

of the flask within a small paper boat; the cork was inserted into the throat of the flask, and the flask tipped into vertical position; the small boat fell to the bottom and the powders were mixed by vigorous shaking of the flask. Thus, the loss of gas was avoided in this case, if reaction started immediately upon direct contact. If reaction did not proceed at room temperature, or if it was in process but the water flow from the gasometer had already ceased, the flask was then placed in a water bath which was gradually heated to boiling, and the reacting mixture was kept on the boiling water bath until the water flow from the gasometer ceased completely; subsequently, the flask was cooled to room temperature, the pressure in the two vessels equalized by the usual procedure, and the volume of displaced water determined, i.e., the gas volume evolved in the 20 to 100° range, and at an external temperature of 100°. The flask was then transferred to a sand bath; the bath temperature was gradually raised to 200°; at this temperature the experiment was continued, until water ceased to flow from the gasometer, and again, the volume of water displaced in the 100-200° interval and at an external temperature of 200°, was measured as in the first case. In each experiment, a qualitative analysis of the gas was carried out to confirm the presence of hydrogen.

The hydrogen volume was not brought to normal pressure, since the error of the experiment, due to uneven mixing, was considerably greater than the correction. It was considered that the hydrogen had been collected at 760 mm pressure, and correction was made only for temperature. Correction for humidity was not made either. Therefore, the experimental data cannot correspond to absolute values, and are used by the authors only for comparative evaluation.

The Effect of the Relative Weight of Beryllium

The completeness of reaction between solid bodies depends upon contact surface; thus, by increasing the relative weights of beryllium, we are creating favorable conditions for hydrogen evolution.

This is confirmed by the following series of experiments (Table 1).

TABLE 1

Expt. Nos.	Crystallohydrate Formula	Weighed Portion		Quantity of Be (equiv)	Evolved H_2 (ml) to 100° and at 100°	H_2 (ml) to 200° and at 200°	H_2 (ml) volume at 0°	H_2O molecules entered into reaction.
		of salt	Be					
40	$K_4Cr_2(SO_4)_4 \cdot 24H_2O$	2.5	0.27	1	87	43	124.3	4.44
		2.5	0.54	2	115	70	172.3	6.16
53	$CoCl_2 \cdot 6H_2O$	1.19	0.13	1	113	120	215.3	3.84
		1.19	0.27	2	85	250	313.3	5.59
		1.19	0.40	3	165	225	360.9	6.45
47	$(NH_4)_2Fe_2(SO_4)_4 \cdot 24H_2O$	2.41	0.27	1	160	10	161.1	5.74
		2.41	0.54	2	160	65	211.8	7.56
23	$CdCl_2 \cdot 2^{1/2}H_2O$	2.88	0.11	1	150	75	208.22	1.89
		2.88	0.23	2	225	165	360.9	3.22
		2.88	0.34	3	165	200	339.63	3.03
37	$SnCl_2 \cdot 2H_2O$	2.26	0.09	1	95	55	142.2	1.28
		2.26	0.14	1.5	95	95	176.4	1.58
		2.26	0.18	2	185	140	301.8	2.78
		2.26	0.27	3	215	175	362.1	3.24
44	$FeCl_3 \cdot 6H_2O$ (yellow)	1.35	0.14	1	165	110	227.5	4.06
		1.35	0.20	1.5	225	167	364.0	6.50
		1.35	0.27	2	265	155	390.0	6.96
		1.35	0.34	2.5	Gas collection unsuccessful; gas evolu-			
		1.35	0.40	3	tion so violent gasometer breaks.			
45	$FeSO_4 \cdot 7H_2O$	1.39	0.16	1	0	0	—	—
		1.39	0.32	2	0	0	—	—
		1.39	0.48	3	0	0	—	—
3	$Na_2SO_3 \cdot 7H_2O$	1.26	0.16	1	0	0	—	—
		1.26	0.32	2	0	0	—	—
5	$Na_2B_4O_7 \cdot 10H_2O$	3.81	0.45	1	0	0	—	—
		3.81	0.90	2	0	0	—	—

An increase in the relative weight of beryllium causes an increase in volume of hydrogen evolution. In those cases where intense reaction proceeded, with large heat evolution, and the mixture heated up strongly, as took place with the chlorides of cobalt, cadmium, divalent lead and trivalent iron (Experiments 53, 23, 37 and 44), a

large excess of beryllium, of two or more equivalents — produced hydrogen evolution in volume exceeding the theoretical possible, according to the reaction:

$$Be + 2HOH' \longrightarrow Be(OH)_2 + H_2.$$ (I)

TABLE 2

Expt. Nos.	Crystallohydrate formula	Weighed portion		Quantity of Be (equiv)	H_2 (ml) evolved		H_2(ml) volume at 0°	H_2O molecules entered into reaction.
		salt	Be		to 100°	to 200°		
1	2	3	4	5	6	7	8	9
1	$Na_2CO_3 \cdot 10H_2O$	1.43	0.45	2	25	0	23.13	0.41
2	$Na_2SO_4 \cdot 10H_2O$	1.61	0.45	2	0	0	—	—
3	$Na_2SO_3 \cdot 7H_2O$	1.26	0.32	2	0	0	—	—
4	$Na_2S_2O_3 \cdot 5H_2O$	2.48	0.45	2	12	0	—	—
5	$Na_2HPO_4 \cdot 12H_2O$	1.79	0.54	2	15	0	11.2	0.10
6	$Na_2B_4O_7 \cdot 10H_2O$	3.81	0.90	2	0	0	13.9	0.13
7	$NaC_2H_3O_2 \cdot 3H_2O$	1.36	0.27	2	0	0	—	—
8	$Na_2[Fe(CN)_5NO] \cdot 2H_2O$	2.89	0.18	2	0	0	—	—
9	$NaC_4H_4O_6 \cdot 4H_2O$	2.82	0.36	2	0	0	—	—
10	$K_4Fe(CN)_6 \cdot 3H_2O$	4.22	0.27	2	0	0	—	—
11	$K_2B_4O_7 \cdot 5H_2O$	1.62	0.23	2	0	0	—	—
12	$(NH_4)_3C_6H_5O_7 \cdot H_2O$	2.61	0.09	2	0	0	—	—
13	$(NH_4)_2C_2O_4 \cdot H_2O$	1.24	0.09	2	0	0	—	—
14	$MgSO_4 \cdot 7H_2O$	2.46	0.63	2	0	0	—	—
15	$Mg(NO_3)_2 \cdot 6H_2O$	1.28	0.27	2	0	0	—	—
16	$MgCl_2 \cdot 6H_2O$	2.03	0.54	2	0	320	293.9	2.62
17	$Ca(NO_3)_2 \cdot 4H_2O$	2.63	0.36	2	0	0	—	—
18	$Ca(C_2H_3O_2)_2 \cdot 2H_2O$	1.94	0.18	2	0	15	13.9	0.13
19	$BaCl_2 \cdot 2H_2O$	2.44	0.18	2	0	23	21.4	0.19
20	$ZnSO_4 \cdot 7H_2O$	2.88	0.63	2	230	0	213.6	1.9
21	$Zn(C_2H_3O_2)_2 \cdot 2H_2O$	2.19	0.18	2	0	0	—	—
22	$Zn(NO_3)_2 \cdot 6H_2O$	2.98	0.54	2	0	0	—	—
23	$CdCl_2 \cdot 2^{1/2} H_2O$	2.88	0.23	2	225	165	360.9	3.22
24	$CdSO_4 \cdot 8^{1/3} H_2O$	2.57	0.24	2	55	15	64.78	0.58
25	$Cd(NO_3)_2 \cdot 4H_2O$	1.54	0.18	2	0	0	—	—
26	$CuCl_2 \cdot 2H_2O$	3.41	0.36	2	180	175	330.8	1.48
27	$CuSO_4 \cdot 5H_2O$	2.5	0.45	2	125	25	140.7	1.26
28	$Cu(NO_3)_2 \cdot 6H_2O$	2.96	0.54	2	0	0	—	—
29	$Cu(C_2H_3O_2)_2 \cdot H_2O$	3.99	0.18	2	0	35	32.28	0.15
30	$Cu(NH_3)_4Cl_2 \cdot H_2O$	2.21	0.09	2	0	0	—	—
31	$Cu(NH_4)_2(SO_4)_2 \cdot 6H_2O$	4.0	0.54	2	260	10	249	2.22
32	$Cu(NH_4)_2Cl_4 \cdot 2H_2O$	2.78	0.18	2	160	190	322.91	2.88
33	$Bi(NO_3)_3 \cdot 5H_2O$	3.05	0.45	2	0	0	—	—
34	$Al_2(SO_4)_3 \cdot 18H_2O$	3.33	0.81	2	225	50	253.6	4.53
35	$K_2Al_2(SO_4)_4 \cdot 24H_2O$	1.19	0.27	2	50	43	87.3	6.24
36	$(NH_4)_2Al_2(SO_4)_4 \cdot 24H_2O$	1.13	0.27	2	48	52	93.0	6.64
37	$SnCl_2 \cdot 2H_2O$	2.26	0.18	2	185	140	301.8	2.78
38	$CrCl_3 \cdot 6H_2O$	1.33	0.27	2	125	225	328.0	5.86
39	$Cr_2(SO_4)_3 \cdot 18H_2O$	3.57	0.81	2	0	0	—	—
40	$K_2Cr_2(SO_4)_4 \cdot 24H_2O$	2.50	0.54	2	115	70	172.3	6.16
41	$Cr(NO_3)_3 \cdot 9H_2O$	2.00	0.40	2	0	0	—	—
42	$Pb(C_2H_3O_2)_2 \cdot 3H_2O$	3.25	0.27	2	0	0	—	—
43	$HgNO_3 \cdot H_2O$	5.61	0.18	2	0	0	—	—
44	$FeCl_3 \cdot 6H_2O$	1.35	0.27	2	265	155	390.0	6.96
45	$FeSO_4 \cdot 7H_2O$	1.39	0.32	2	0	0	—	—

In those cases where reaction with an equivalent weight of beryllium does not take place, a relative increase in the beryllium does not cause reaction (Experiments 45, 3 and 6).

On the basis of orientative experiments, the author has investigated the interaction of beryllium with fifty-nine solid crystallohydrates, representing combinations of twenty-three cations and seventeen anions. In all instances, to obtain comparative results, the weight of beryllium powder taken was twice that of the the calculated theoretical, according to Reaction (I).

All experiments were conducted in

| Expt. Nos. | Crystallohydrate formula | Weighed portion | | Quantity of Be (equiv) | H_2(ml) evolved | | H_2(ml) volume at 0° | H_2O molecules entered into reaction |
		salt	Be		to 100°	to 200°		
1	2	3	4	5	6	7	8	9
46	$Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$	3.92	0.54	2	0	80	74.5	0.67
47	$(NH_4)_2Fe_2(SO_4)_4 \cdot 24H_2O$	2.41	0.54	2	160	65	211.8	7.56
48	$Fe(NO_3)_3 \cdot 9H_2O$	4.04	0.81	2	0	0	—	—
49	$FePO_4 \cdot 2H_2O$	1.87	0.18	2	0	0	—	—
50	$Fe_3(PO_4)_2 \cdot 8H_2O$	2.51	0.36	2	0	0	—	—
51	$NiSO_4 \cdot 7H_2O$	2.80	0.63	2	0	0	—	—
52	$Ni(NH_4)_2 (SO_4)_2 \cdot 6H_2O$	3.95	0.54	2	0	0	—	—
53	$CoCl_2 6H_2O$ calculated with HCl	1.19	0.27	2	85	250	313.3 +14.5	5.59 5.86
54	$CoSO_4 \cdot 7H_2O$	0.84	0.19	2	0	0	—	—
55	$Co(NO_3)_2 \cdot 6H_2O$	2.91	0.54	2	0	0	—	—
56	$Co(C_2H_3O_2)_2 \cdot 4H_2O$	2.49	0.36	2	36	8	41.0	0.37
57	$MnCl_2 \cdot 4H_2O$	1.98	0.36	2	0	115	109	0.97
58	$Mn(NO_3)_2 \cdot 6H_2O$	1.44	0.27	2	0	0	—	—
59	$Ba(OH)_2 \cdot 8H_2O$	3.16	0.72	2	360	5	333.26	2.98

multiple repetition.

Results of the experiments are quoted in Table 2.

Analysis of the Experimental Results

In Table 2 are collected the results obtained from the study of fifty-nine various crystallohydrates with beryllium powder.

All calculations for the quantity of water of crystallization entering into reaction were made according to the equation $Be + 2H^{\cdot}OH^{\cdot} = Be(OH)_2 + H_2$, in contradistinction to which there were obtained values considerably exceeding the possible theoretical in a number of cases. This was done for the purpose of comparing the results obtained by the author with the results of Mikhailenko and Semishin, using magnesium, aluminum and zinc, where the calculations were made according to the above-quoted equation.

I. In four instances (Experiments 23, 32, 37 and 44) the quantity of water of crystallization entered into reaction was more than 100%. These are the cases where the reaction started with a sudden impetus and with considerable heating up. It could be assumed that due to the high temperature developed at the abrupt start of the reaction, as a result of the reaction of beryllium with the crystallization water of the crystallohydrates, the beryllium hydroxide formed decomposed with liberation of water $Be(OH)_2 = BeO + H_2O$, since beryllium hydroxide can stand drying up to 100°, but upon stronger heating splits off water, transforming into BeO. In its turn the water liberated from $Be(OH)_2$ entered into reaction with the beryllium powder, for which reaction the catalyst was the salt contained in the reaction mixture. The author is basing this assumption upon the work of Mikhailenko and Mushinski, who demonstrated that the catalyst for the reaction of metallic magnesium with water appeared to be those substances whose crystallohydrates react with magnesium, and also upon the following observations which have been made in the process of the author's work.

1) Upon heating a mixture of the crystallohydrate powder with beryllium powder, considerable water condensed on the wall of the flask in a number of instances. When this water, running down the walls of the flask, dropped onto the mixture, this provoked an intense evolution of hydrogen in some cases, for example, in the experiments with $CuSO_4 + 5H_2O$ (experiment 27), with $CuCl_2 \cdot 6H_2O$ (experiment 52); in other instances the dropping of water onto the crystallohydrate and beryllium mixture remained without results, even upon heating to 200°, as for example with $Zn(C_2H_3O_2)_2 \cdot 2H_2O$ (experiment 21), with $K_4Fe(CN)_6 \cdot 3H_2O$ (experiment 10) and with $Na_2B_4O_7 \cdot 10H_2O$ (experiment 6). Thus, as regards the reaction of beryllium with water, the catalytic salts for the reaction could be non-catalytic.

2) In two cases (experiment 23 with $CdCl_2 \cdot 2^{1/4}\ H_2O$ and experiment 24 with $CdSO_4 \cdot {}^{8/3}\ H_2O$) there was an intensive evolution of hydrogen without a heating up of the mixture, upon wetting with water the mass which had remained in the flask after cessation of the previous hydrogen evolution due to the 200° heating.

In the remaining instances, such observations were not made, therefore, it is not possible to say anything definite, but in any case there is still the phenomenon of reaction activation between the metal and water.

3) Some salts which are devoid of crystallization water do not react with beryllium powder in the dry state, but when moist, or in the form of a water suspension, react with hydrogen evolution. Thus, for example, a water suspension of Cu_2Cl_2 with beryllium powder gives an intense reaction, with heat and violent hydrogen evolution, hydrogen chloride, and copper reduction.

4) In some instances the crystallohydrates, reacting with beryllium powder only upon heating (Experiment 24 with $CdSO_4 \cdot {}^{8/3}\ H_2O$ and experiment 27 with $CuSO_4 \cdot 5H_2O$) react very vigorously in the moist state without heating, with an evolution of heat for the overall mass, violent evolution of hydrogen, and metal reduction.

The cases quoted can be summed up in the conception of the reaction activation of beryllium with water. It was of great interest and important, to explain the mechanism of activation, and to clarify the role of the activator in the reaction. Investigation of the reaction products could have given results in this sense, however, investigation of the mixture in this direction was not carried out. The authors will utilize the observed activation phenomenon only to base their assumption about the process of hydrogen evolution from the mixture of crystallohydrate with beryllium powder in those cases where the hydrogen evolution is greater than that theoretically possible according to the standard reaction scheme between metal and water. It is possible that in the remainder of the cases where heating was conducted at 200° the process went analogously, but less intensely, and thus the amount of crystallization water entering into reaction with beryllium did not exceed 100%. Without an investigation of the reaction products it is difficult to express anything more definite.

II. The influence of the nature of the crystallohydrate upon the beryllium activity as regards crystallization water was very clearly shown. In some cases reaction occurred upon mixing, in other cases upon light heating, and in still others reaction did not occur even upon heating to 200°; sometimes hydrogen was evolved very slowly and gradually, in other cases the hydrogen evolution proceeded very violently, occasionally with explosion-like violence; the intensity of the reaction occasionally shows two or three maxima (experiment 37 with $SnCl_2 \cdot 2H_2O$ and experiment 44 with $FeCl_3 \cdot 6H_2O$, and others).

The last case indicates that the various molecules with added neutral water have bonds in the aqua-complex of unequal stability with an ion-complexing agent, and consequently with varying degree of proton mobility.

Semishin has expressed the assumption that in the inner sphere of the aqua-complex the water molecules are arranged in layers, distinguished by attraction energy of the neutral addendum, starting from the fact that neither he, nor Mikhailenko, have been able to induce interaction between powdered Mg, Al or Zn metal with more than 50% of the crystallization water. The maxima in the intensity of crystallohydrate reaction with beryllium, observed by the author, confirm this assumption.

The absence of interaction between beryllium and crystallohydrate water was established in thirty-two instances out of fifty-nine; six crystallohydrates started to react at temperatures above 100°, (experiments 16, 18, 19, 29, 46 and 57); of four, the reaction terminated at 100°, and further heating to 200° did not procure reaction (tests 1, 4, 5, 20); in six cases reaction started within a few seconds after mixing, with sudden violence and heat evolution of the mixture (tests 23, 26, 37, 44, 53); in the remainder of cases reaction proceeded with moderate speed, starting in the interval 40-70°. The rate of hydrogen evolution for a series of crystallohydrates has two maxima: a first one up to 100°, and a second between 100 and 200°. The quantity of crystallization water entering into reaction fluctuates from 1.03% in $Na_2HPO_4 \cdot 12H_2O$, to 97.62% in $CrCl_3 \cdot 6H_2O$, not counting those four crystallohydrates whose quantity of water entered into reaction exceeds 100% (tests 23, 32, 37, 44). Thus we see that the nature of the crystallohydrates affects the results of the reaction with extraordinarily large magnitude. In order to better ascertain the influence of the crystallohydrate nature, they were grouped into several tables according to the anions.

As table 3 shows, of the chlorides, the crystallohydrates of the metals belonging to the iron family, and salts of the so-called heavy metals, enter most actively into reaction. The very small activity of the $MnCl_2 \cdot 4H_2O$

TABLE 3

Expt. No.	Crystallohydrate formula	Volume H_2(ml) at 0°	H_2O molecules entered into reaction
1	2	3	4
16	$MgCl_2 \cdot 6H_2O$	293.9	2.62
19	$BaCl_2 \cdot 2H_2O$	21.4	0.19
23	$CdCl_2 \cdot 2\frac{1}{2}H_2O$	360.9	3.22
26	$CuCl_2 \cdot 2H_2O$	330.8	1.48
37	$SnCl_2 \cdot 2H_2O$	301.8	2.78
38	$CrCl_3 \cdot 6H_2O$	328.0	5.86
44	$FeCl_3 \cdot 6H_2O$	390.0	6.96
53	$CoCl_2 \cdot 6H_2O$	313.3	5.59
57	$MnCl_2 \cdot 4H_2O$	109.0	0.97
32	$Cu(NH_4)_2Cl_4 \cdot 2H_2O$	322.91	2.86
30	$Cu(NH_3)_4Cl_2 \cdot H_2O$	0	0

TABLE 4

Expt. No.	Crystallohydrate formula	Volume H_2(ml) at 0°	H_2O molecules entered into reaction
1	2	3	4
2	$Na_2SO_4 \cdot 10H_2O$	0	0
14	$MgSO_4 \cdot 7H_2O$	0	0
20	$ZnSO_4 \cdot 7H_2O$	213.6	1.9
24	$CdSO_4 \cdot \frac{8}{3}H_2O$	64.78	0.58
27	$CuSO_4 \cdot 5H_2O$	140.7	1.26
31	$Cu(NH_4)_2(SO_4)_2 \cdot 6H_2O$	249	2.22
34	$Al_2(SO_4)_3 \cdot 18H_2O$	253.6	4.53
35	$K_2Al_2(SO_4)_4 \cdot 24H_2O$	87.3	6.24
36	$(NH_4)_2Al_2(SO_4)_4 \cdot 24H_2O$	93.0	6.64
39	$Cr_2(SO_4)_3 \cdot 18H_2O$	—	0
40	$K_2Cr_2(SO_4)_4 \cdot 24H_2O$	172.3	6.16
45	$FeSO_4 \cdot 7H_2O$	—	0
46	$Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$	74.5	0.67
47	$(NH_4)_2Fe_2(SO_4)_4 \cdot 24H_2O$	211.8	7.56
51	$NiSO_4 \cdot 7H_2O$	—	0
52	$Ni(NH_4)_2(SO_4)_2 \cdot 6H_2O$	—	0
54	$CoSO_4 \cdot 7H_2O$	—	0

represents an exception. The chlorides of the alkaline earth metal crystallohydrates display little activity, and of all the chlorides investigated, only the chloride of copper ammoniate failed to react at all with beryllium.

A comparison of data in tables 3 and 4 demonstrates that the crystallohydrates of the sulfates are considerably less reactive toward beryllium than the crystallohydrates of the chlorides. Of eleven investigated chlorides, only one, the chloride of copper ammoniate, failed to react with beryllium, and only had a percentage of water of crystallization entered into reaction which was less than 10%, the majority having a percentage considerably higher 50 to that approaching 100% and four leaving considerably higher than 100%. And at the same time, of the seventeen sulfates investigated, seven did not react with beryllium, and the remaining had a quantity of percentage water of crystallization entered into reaction which did not exceed 37%, with one exception; in the majority of cases (seven out of nine) this percentage fluctuated from 21 to 27%. Among the sulfates, the inactive proved to be the crystallohydrates of sodium, magnesium, chromium, and also all of the metals of the iron family.

Double salts and alums displayed greater activity than the simple ones. Thus, for example, $Cr_2(SO_4)_3 \cdot 18H_2O$ does not react, but in potassium chromate alum it was possible to decompose 25% of the water of crystallization. This phenomenon is also observed among the chlorides, $CuCl_2 \cdot 2H_2O$ gives 73.84% of water entered into reaction, and $Cu(NH_4)_2Cl_4 \cdot 2H_2O$ -144.15%. The exception to this situation is nickel, for which the sulfate — both simple and double with ammonia — does not react with beryllium.

Thus, the crystallohydrates of the sulfates in all cases manifest less activity with beryllium as compared with the chlorides, exactly the same as was noted in the works of Mikhailenko and Semishin with magnesium, aluminum and zinc.

In experiments 22, 23, 41, 43, 48 and 58, considerable volume of gas was collected (from 50 to 135 ml), but it was found to be pure nitric oxide. Thus, from the eleven investigated nitrates not one reacted with beryllium to evolve hydrogen. The presence in the crystallohydrate of the nitrate ion renders it entirely inactive as regards to beryllium.

From a comparison of the data in tables 6 and 4, it can be seen that the anion of acetic acid, in all cases except one (test 56), exerts an inhibitory action upon the interaction of the crystallohydrate with beryllium which is considerably greater than that of the $SO_4^=$ ion.

The anions can be arranged in a sequence, according to decreasing activity, as regards the effect of the anion upon the activity of the crystallohydrate with beryllium:

$$Cl' > SO_4^= > (C_2H_3O_2)' > NO_3'$$

TABLE 5

Nitrates

Test No.	Crystallohydrate formula	Total H_2 separated (in ml)
15	$Mg(NO_3)_2 \cdot 6H_2O$	0
17	$Ca(NO_3)_2 \cdot 4H_2O$	0
22	$Zn(NO_3)_2 \cdot 6H_2O$	0
25	$Cd(NO_3)_2 \cdot 4H_2O$	0
28	$Cu(NO_3)_2 \cdot 6H_2O$	0
33	$Bi(NO_3)_3 \cdot 5H_2O$	0
41	$Cr(NO_3)_3 \cdot 9H_2O$	0
43	$HgNO_3 \cdot H_2O$	0
48	$Fe(NO_3)_3 \cdot 9H_2O$	0
55	$Co(NO_3)_2 \cdot 6H_2O$	0
58	$Mn(NO_3)_2 \cdot 6H_2O$	0

TABLE 6

Acetates

Test No.	Crystallohydrate formula	H_2 vol. (ml at 0°)	H_2O molecules entered into reaction
7	$NaC_2H_3O_2 \cdot 3H_2O$	0	0
18	$Ca(C_2H_3O_2)_2 \cdot 2H_2O$	13.9	0.13
21	$Zn(C_2H_3O_2)_2 \cdot 2H_2O$	0	0
29	$Cu(C_2H_3O_2)_2 \cdot H_2O$	32.28	0.15
42	$Pb(C_2H_3O_2)_2 \cdot 3H_2O$	0	0
56	$Co(C_2H_3O_2)_2 \cdot 4H_2O$	41.0	0.37

This sequence we arranged on the basis of a study of the reaction with beryllium of ten crystallohydrates with the Cl^- ion, seventeen with the $SO_4^=$ ion and six with the $(C_2H_3O_2)'$ ion, and eleven with the NO_3^- ion. The remaining fifteen crystallohydrates are found to be salts of various cations and anions repeated once or twice in the tests. Thus, as for an arrangement of similar type for all of the anions, there are insufficient data for the time being.

On the basis of the data in table 7, it can be assumed that the $PO_4^{\equiv}$ ion and the organic acid anions will, as a rule, exert an inhibitory effect on the reaction.

TABLE 7

Crystallohydrates of the Salts of Various Acids

Test No.	Crystallohydrate formula	H_2 vol. (ml) at 0°	H_2O molecules entered into reaction	Test No.	Crystallohydrate formula	Vol. of H_2 (ml) at 0°	H_2O molecules entered into reaction
1	$Na_2CO_3 \cdot 10H_2O$	23.13	0.41	10	$K_4Fe(CN)_6 \cdot 3H_2O$	—	0
3	$Na_2SO_3 \cdot 7H_2O$	—	0	11	$K_2B_4C_7 \cdot 5H_2O$	—	0
4	$Na_2S_2O_3 \cdot 5H_2O$	11.2	0.10	12	$(NH_4)_3C_6H_5O_7 \cdot H_2O$	—	0
5	$Na_2HPO_4 \cdot 12H_2O$	13.9	0.13	13	$(NH_4)_2C_2O_4 \cdot H_2O$	—	0
6	$Na_2B_4O_7 \cdot 10H_2O$	—	0	49	$FePO_4 \cdot 2H_2O$	—	0
8	$Na_2[Fe(CN)_5NO] \cdot 2H_2O$	—	0	50	$Fe_3(PO_4)_2 \cdot 8H_2O$	—	0
9	$NaKC_4H_4O_6 \cdot 4H_2O$						

As regards the activity of beryllium with the crystallohydrates, in comparison with magnesium, aluminum and zinc, the beryllium fails to react with a great many more crystallohydrates than the metals mentioned, but in those cases where reaction does occur, beryllium reacts with considerable more activity than the metals mentioned.

The table 8 which follows illustrates this situation.

TABLE 8

Metals	The number of investigated crystallohydrates	The number of crystallohydrates		Crystallohydrate percent, where H_2O entered into reaction $> 10\%$	Maximum % of H_2O entered into reaction	Crystallohydrate formula, from which the maximum of H_2O was successfully split.
		Non-reacting	Reacted			
Be	59	31	28	75	144.15	$Cu(NH_4)_2Cl_4 \cdot 2H_2O$
Mg	53	3	50	44	39.1	$CoCl_2 \cdot 6H_2O$
Al	42	8	34	23.5	51.3	$FeCl_3 \cdot 4H_2O$
Zn	43	5	38	11.5	29.3	$NiCl_2 \cdot 6H_2O$

TABLE 9

Interaction of the Crystallohydrates of the Chlorides with Be, Mg, Al and Zn at 200°

No.	Crystallohydrate formula	Entered into reaction with the water of crystallization							
		Be (Alekseeva data)		Mg (Mikhailenko data)		Al (Semishin data)		Zn (Semishin data)	
		%	Mol.	%	Mol.	%	Mol.	%	Mol.
1	$MgCl_2 \cdot 6H_2O$	43.42	2.62	11.87	0.7	1.63	0.10	1.3	0.08
2	$BaCl_2 \cdot 2H_2O$	9.55	0.19	0	0	3.6	0.07	2.99	0.06
3	$CdCl_2 \cdot 2^1/_2H_2O$	128.9	3.22	Vigorous reaction upon grinding		7.1	0.14	Vigorous reaction upon grinding	
4	$CuCl_2 \cdot 2H_2O$	73.84	1.48	5.8	0.12	8.6	0.17	5.6	0.11
5	$SnCl_2 \cdot 2H_2O$	134.74	2.78	Vigorous reaction upon grinding		21.8	0.44	(8.0)	(0.16)
6	$CrCl_3 \cdot 6H_2O$	97.62	5.86	21.11	1.27	Vigorous reaction upon grinding		(5.94)	(0.36)
7	$FeCl_3 \cdot 6H_2O$	116.17	6.98	Vigorous reaction upon grinding		22.1	1.33	6.6	0.40
8	$CoCl_2 \cdot 6H_2O$	93.16	5.59	39.19	2.35	31.7	1.90	22.9	1.37
9	$NiCl_2 \cdot 6H_2O$	—	—	25.35	1.34	24.7	1.48	29.3	1.76
10	$MnCl_2 \cdot 4H_2O$	24.33	0.97	25.25	1.01	1.30	0.07	5.8	0.23
11	$FeCl_2 \cdot 4H_2O$	—	—	28.56	1.14	51.3	2.05	9.1	0.36
12	$Cu(NH_4)_2Cl_4 \cdot 2H_2O$	144.15	2.88	—	—	—	—	—	—

TABLE 10

Interaction of the Crystallohydrates of the Sulfates with Be, Mg, Al and Zn

No.	Crystallohydrate formula	Entered into reaction with the water of crystallization							
		Be (Alekseeva data)		Mg (Mikhailenko data)		Al (Semishin data)		Zn (Semishin data)	
		%	Mol.	%	Mol.	%	Mol.	%	Mol.
1	$Na_2SO_4 \cdot 10H_2O$	0	0	3.64	0.36	1.5	0.15	0	0
2	$CaSO_4 \cdot 2H_2O$	—	—	0	0	—	—	—	—
3	$MgSO_4 \cdot 7H_2O$	0	0	7.21	0.50	2.1	0.15	1.7	0.12
4	$ZnSO_4 \cdot 7H_2O$	27.24	1.9	23.5	1.63	1.5	0.1	1.0	0.07
5	$CdSO_4 \cdot {}^8/_3 H_2O$	21.67	0.58	6.21	0.50	0	0	3.4	0.27
6	$CuSO_4 \cdot 5H_2O$	25.13	1.26	5.63	0.28	1.4	0.07	1.2	0.06
7	$MnSO_4 - 5H_2O$	—	—	12.3	0.86	0.89	0.04	0.72	0.04
8	$FeSO_4 \cdot 7H_2O$	0	0	0	0	0	0	2.8	0.2
9	$NiSO_4 \cdot 7H_2O$	0	0	4.08	0.28	2.7	0.19	—	—
10	$CoSO_4 \cdot 6H_2O$	0	0	9.44	0.57	0	0	1.04	0.06
11	$Al_2(SO_4)_3 \cdot 18H_2O$	25.16	4.53	6.44	1.16	0.90	0.1	1.99	0.36
12	$K_2Al_2(SO_4)_4 \cdot 24H_2O$	26.0	6.24	17.39	4.17	2.90	0.59	2.23	0.54
13	$Cr_2(SO_4)_3 \cdot 18H_2O$	0	0	—	—	—	—	0	0
14	$K_2Cr_2(SO_4)_4 \cdot 24H_2O$	25.65	6.16	15.73	3.78	1.38	0.33	1.8	0.43
15	$(NH_4)_2Fe_2(SO_4)_4 \cdot 24H_2O$	31.52	7.56	—	—	0	0	1.20	0.29
16	$(NH_4)_2Fe(SO_4)_2 \cdot 6H_2O$	11.09	0.67	8.14	0.49	0	0	1.3	0.08

In all cases the beryllium activity, as regards the crystallohydrates of the chlorides, exceeds the activity of aluminum and zinc many-fold, and exceed considerably the magnesium activity, and only as regards the $MnCl_2 \cdot 4H_2O$, are the activity of the beryllium and the magnesium the same (table 9).

For the sulfates, the picture obtained is somewhat different (table 10).

As the data of table 10 show, this picture is considerably variegated. Thus, $MgSO_4 \cdot 7H_2O$ and $NiSO_4 \cdot 7H_2O$ do not give reaction with beryllium but react with the remaining three metals; $CdSO_4 \cdot {}^3/_2H_2O$, Mohr's salt and ammonia · the ferric alums of these '... t react only with aluminum but $FeSO_4 \cdot 7H_2O$ on the contrary, reacts only with zinc; $Na_2SO_4 \cdot 10H_2O$, does not react with zinc or beryllium. For all four metals the interaction with the various crystallohydrates of the sulfate is clearly seen to be an inhibitory role for the SO_4'' ion, in contrast to the Cl' ion.

For the salt series there is greater activity of beryllium, as regards the sulfates, than of aluminum and zinc, and even of magnesium, but in this last situation there are exceptions, where the beryllium does not react and the magnesium displays activity — these are the sulfates of sodium, magnesium, cobalt and nickel.

SUMMARY

1. Metallic beryllium powder reacts with the water of crystallization of solid crystallohydrates.

2. One of the reaction products is found to be hydrogen.

3. The quantity of crystallohydrate water which enters into reaction is increased with an increase in the relative amount of beryllium, but within certain limits.

4. The reaction of beryllium with water can be activated at ordinary temperatures both by crystallohydrates reacting in the solid state with beryllium and by some anhydrous, practically water-insoluble salts.

5. The basic reaction between beryllium and the water of crystallization, which proceeds according to the scheme $Be + 2HOH' \longrightarrow Be(OH)_2 + H_2$, is complicated in those cases where the process occurs with considerable heating of the reaction mixture, in that $Be(OH)_2$ loses water, and the evolving water is decomposed by the metallic beryllium under the activating influence of the crystallohydrate.

6. In a number of cases, upon reaction of beryllium with the crystallohydrates of chlorides, there is observed, along with hydrogen, the evolution of hydrogen chloride, and the reduction of the salt cation to the metal.

7. The nature of the crystallohydrate affects the intensity of the reaction to an extreme degree. The quantity of water entered into reaction fluctuates from zero to 144%. Some crystallohydrates enter into reaction with beryllium upon direct contact, others require heating to various degrees, and yet others do not react, even when heated up to 200°.

8. The crystallohydrates of the chlorides possess the greatest activity with beryllium.

9. The crystallohydrates of the nitrates are entirely inactive toward beryllium.

10. The presence of the SO_4'' ion in the crystallohydrate and $(C_2H_3O_2)'$ strongly decrease the activity of the crystallohydrates toward beryllium, and at the same time, the presence of the $(C_2H_3O_2)'$ ion decreases the activity to a greater degree than the SO_4'' ion.

11. The crystallohydrates of the double salts and of alum react with beryllium more actively than the corresponding simple salts.

12. Of the cations, those of sodium and the alkaline earth metals impart the smallest activity to the crystallohydrates. The chlorides of the metals of the iron family and the heavy metals possess the greatest activity. The most active of the simple salts are: $SnCl_2 \cdot 2H_2O$, $CdCl_2 \cdot 2^1/_2H_2O$, $FeCl_3 \cdot 6H_2O$, $CrCl_3 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ and $CuCl_2 \cdot 2H_2O$.

13. In all cases beryllium is considerably more active toward the crystallization water of the solid crystallohydrates of chloride, than are magnesium, aluminum and zinc. According to decreasing activity, these metals are arranged in the sequence Be—Mg—Al—Zn.

14. Regardless of the great activity of beryllium, it is not possible to decompose all of the water of crystallization in a majority of the crystallohydrates. The interaction of a crystallohydrate with beryllium occurs stepwise, the intensity of hydrogen evolution having two, and in some cases three, maxima for the majority of crystallohydrates.

All of this taken together, confirms the position of Semishin that "the water molecules in the aquo-complex are unequal, that they are arranged in water layers within the internal sphere of the complex, differing by the energy of addition and by the degree of mobility of the proton [5]".

LITERATURE CITED

[1] Ya. I. Mikhailenko, Trans. of the 1st Mendeleev Congress, .., Page 317 (1907).

[2] Ya. I. Mihailenko and P. T. Mushinsky, Reports Tomsk Institute Technology 31, 1 (1913).

[3] V. I. Semishin, Reaction of Metallic Zinc with Water of Crystallization, J. Gen. Chem. 10, 319 (1940).

[4] V. I. Semishin, Reaction of Metallic Zinc with Water of Crystallization, J. Gen. Chem. 10, 328 (1940).

[5] V. I. Semishin, Some General Problems on the Structure of Crystallohydrates and Their Properties J. Gen. Chem. 10, 335 (1940).

THERMAL DEPENDENCE OF THE HYDRATION REACTION RATE OF THE METAPHOS-PHORIC ACIDS

I. A. Brovkina

The stereochemical theory of Yu. V. Khodakov [1,2] has been confirmed by the example of phosphoric anhydride hydration in the work of Khodakov and Rodionova [3]. The metaphosphoric acid formed upon hydration of phosphoric anhydride was found to be tetrametaphosphoric acid, i.e., an acid of different nature than the trimetaphosphoric acid.

In the present work the temperature function of the hydration reaction rate of trimeta- and of tetrametaphosphate ions, in alkaline and in acid media, was investigated for the purpose of finding a physico-chemical method for the identification of these meta acids, for they do not differ from one another analytically (all of their salts are soluble).

The hydration reaction, both of the trimetaphosphate and of the tetrametaphosphate ion, is evidently monomolecular, but in diluted aqueous solution the quantity of water used for hydrolysis should be neglected, and the concentration of water considered to be constant, then the speed of reaction will be expressed by the first order equation:

$$K = \frac{2.303}{\tau} \log \frac{a}{a-x},$$

where: a — initial concentration;
$c = (a-x)$ — concentration in the moment of τ;
τ — time, in minutes
K — velocity constant.

The characteristic peculiarities of the equation for first order reactions are that the numerical value for the velocity constant does not depend upon choice of units for concentration, and at the same time the half-life does not depend upon the initial concentration, and can appear as the velocity characteristic of such reactions, the same as the constant. The half-life period can be calculated according to the following formula:

$$\tau_{\frac{1}{2}} = \frac{\log 2}{K} = \frac{0.693}{K}.$$

The reaction rate increases rapidly with temperature.

The dependence of reaction rate upon temperature can be expressed by the equation $\log K = B - \frac{A}{T}$, according to which the value, $\log K$, in the function $\frac{1}{T}$ should be graphically expressed by a straight line, while the tangent of the angle of the straight line with the abscissa axis gives the constant A, and the section cut by it on the ordinate axis gives B.

The constant coefficient, B, is the logarithm of the total number of molecular impacts. The coefficient $A = \frac{E}{2.303R} = \frac{E}{4.575}$, where E = activation energy, i.e., that minimum energy which the molecule should possess in order that the impacts be effective.

The reaction should be preceded by a weakening or break-down of the internal bonds of the reacting molecules, without which, regrouping of the atoms is impossible, to lead to the formation of molecules of reaction products.

Ordinarily the mean energy of the molecules is considerably lower than the activation energy, thus the value of the activation energy is determined only by a few co-impacts of the higher energy-containing molecules.

The number of activated molecules able to react increases with increase in temperature.

If the velocity constants are known for different temperatures from experiment, then the activation energy can be computed according to the equation:

$$E = \frac{RT_2 T_1}{T_2 - T_1} \ 2.303 \log \frac{K_2}{K_1} \ .$$

The hydration reaction of the trimeta- and the tetra-metaphosphates proceed with sufficient speed only in acid or alkaline solution, where they are catalyzed by the H_3O^+ or the OH^- ions. The velocity constant is proportional to the concentration of catalytic ions.

EXPERIMENTAL

Starting materials for execution of the work were sodium trimetaphosphate and tetrametaphosphate.

The trimetaphosphate of sodium was obtained by calcination of the monosubstituted derivative of sodium orthophosphate at a defined temperature rate. The product obtained after calcination was recrystallized and dehydrated in a drying cabinet and over sulfuric acid.

Sodium tetrametaphosphate was prepared by neutralization of a freshly prepared solution of tetrametaphosphoric acid, obtained by dissolving in water the volatile modification of phosphoric anhydride.

The extreme hygroscopicity of the phosphoric anhydride necessitated application, during the work, of a whole series of precautions. In order to obtain pure tetrametaphosphoric acid, the phosphoric anhydride was dissolved in water in small portions, cautiously, to avoid heating up. The acid obtained was titrated, and the whole solution was then neutralized with the calculated quantity of alkali.

The reactions, occurring at the same time, can be expressed by the following equations:

$$P_4O_{10} + 2H_2O = H_4P_4O_{12},$$

$$H_4P_4O_{12} + 4NaOH = Na_4P_4O_{12} + 4H_2O.$$
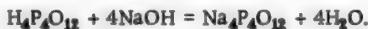
The sodium tetrametaphosphate solution obtained in this manner could be preserved for a few days' duration.

Procedural Method for Conduction of the Hydration Reaction

The hydration reaction of both sodium trimetaphosphate and tetrametaphosphate was carried out in a glass test tube with a dephlegmator and thermostatic heating with an electric heater.

The thermostatic temperature was supported with the help of a thermoregulator with an accuracy of $\pm 0.01^\circ$ C.

Approximately 50 ml of 0.1 N-solution was taken for hydration, to which was added alkali (or acid) in such volume as to maintain in the mixture a concentration 0.1 N with respect to alkali (or acid). After lapse of a given time, from the beginning of heating of the solution, a 5 ml sample was taken which was rapidly cooled and analyzed.

After cooling, the solution of sample taken was neutralized accurately to a pH of 9.2 in the presence of phenolphthalein. An excess of silver nitrate solution was added to the neutral solution for precipitation of the hydration products. Neither trimetaphosphate nor tetrametaphosphate ions precipitate with silver ion, but the hydration products precipitate. The precipitate was filtered off.

1-2 ml of concentrated nitric acid was added to the filtrate to determine the quantity of remaining non-hydrated metaphosphate ions, and the solution was evaporated for 1-1.5 hours on a sand bath (but not to dryness). Upon such lengthy boiling in the presence of the concentrated acid, the m-phosphate ions hydrate fully, and transform into o-phosphate ions.

After cooling, the solution was diluted with water, neutralized to pH 9.2, and the o-phosphate ion precipitated by silver nitrate. At a pH of 9.2 there could only be present in the solution the ions of $HPO_4^=$, which, upon reaction with silver ions, form hydronium ions according to the reaction:

$$H_2O + HPO_4^= + 3 Ag^\cdot = Ag_3PO_4 + H_3O^\cdot \ ,$$

during which the pH of the solution decreases.

The liberated hydronium ions were very accurately titrated with alkali in the presence of phenol red indicator.

From the quantity of alkali used for titration of the hydronium ions, the equivalent concentration of phosphate ion was calculated.

On the basis of the data obtained, kinetic curves were plotted, demonstrating changes in concentration of initial product with time.

The rate constants were then calculated and finally the activation energy of hydration for m-phosphoric acids.

TABLE 1

Hydration of trimetaphosphate in alkaline medium at a temperature of 65°

Time (in min.)	0.0347 N-KOH (ml)	Normality (N) of sample sol.	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0794	100	—
30	7.60	0.0528	66.7	0.0099
65	5.55	0.0387	48.7	0.0111
90	4.92	0.0342	43.0	0.0094
160	2.15	0.0149	18.8	0.0105
			Average K = 0.010	

TABLE 2

Hydration of trimetaphosphate in alkaline medium at a temperature of 75°

Time (in min.)	0.0426 N-KOH (ml)	Normality (N) of sample sol.	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0822	100.0	—
17	6.2	0.0540	65.0	0.024
45	4.4	0.0375	45.5	0.017
68	3.5	0.0300	36.0	0.015
90	2.25	0.0192	23.5	0.016
0	—	0.079	100.0	—
10	8.0	0.067	76.0	0.017
30	5.0	0.426	54.0	0.020
			Average K = 0.022	

TABLE 3

Hydration of trimetaphosphate in alkaline medium at a temperature of 85°

Time (in min.)	0.0347 N-KOH (ml)	Normality (N) of sample sol.	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0788	100.0	—
6	8.20	0.0570	73.0	0.054
22	4.60	0.0320	41.0	0.042
37	2.60	0.0180	26.0	0.040
65	1.20	0.0084	11.0	0.038
			Average K = 0.042	

TABLE 4

Hydration of trimetaphosphate in alkaline medium at a temperature of 90°

Time (in min.)	0.0347 N-KOH (ml)	Normality (N) of sample sol.	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0788	100.0	—
5	4.7	0.0326	42.0	—
18	2.9	0.0199	25.3	0.078
48	0.7	0.0049	6.2	0.077
53	0.2	0.0014	1.8	0.076
			Average K = 0.077	

Experimental Results

The results of experiments on the hydration of trimetaphosphate- and tetrametaphosphate-ions, in alkaline and acid media, at various temperatures, are compiled in the following tables and graphs shown below. In graph 1 of the tables, the time of taking of sample from the start of the reaction is indicated. In graph 2 is indicated the number of milliliters of alkali used for titration of the hydronium ions released upon precipitation of the phosphate ions by silver ions in 5 ml of solution. The concentration of phosphate ion is expressed by the normality of the solution and is quoted in graph 3.

In graph 4 is given the percentage of non-hydrated m-phosphate remaining at the moment of sampling.

In graph 5 are quoted the rate constants for a given temperature and the average speed is deduced.

The concentration changes of m-phosphate with time are pictured in Figs.1, 3 and 5, where a curve corresponds for each temperature. On the abscissa axis, time is marked (in minutes), and on the ordinate axis - the percentage of nonhydrated metaphosphate ion remaining.

I. The hydration reaction of trimetaphosphate in alkaline solution was studied at temperatures of 65, 75, 85 and 90°. The alkalinity of the solutions was about 0.1 normal. 25 ml of the solution was taken for reaction.

The results of the experiments, and the calculated rate constants, are cited in Tables1, 2, 3 and 4.

The monomolecularity of the trimetaphosphate hydration reaction was examined by means of the curves of Fig.1. Good agreement for half-life periods found graphically, with half-life periods calculated according to the formula: $\tau_{\frac{1}{2}} = \dfrac{\log 2}{K}$, quoted in Table 5, was obtained.


Fig. 1. Hydration reaction of trimetaphosphate in alkaline medium. 1 - at 65°; 2 - at 75°; 3 - at 85°; 4 - at 90°.

TABLE 5

Half-life period for the trimetaphosphate ion in alkaline medium

Temp. (°C)	Rate Constant	$\dfrac{\log 2}{K}$	Half-life period in minutes	
			Calculated theoretically	Found by curves
65	0.010	$\dfrac{0.693}{0.010}$	69.3	65
75	0.022	$\dfrac{0.693}{0.022}$	34.6	38
85	0.042	$\dfrac{0.693}{0.042}$	18.0	17
90	0.077	$\dfrac{0.693}{0.077}$	8.0	7

TABLE 6

Relation of rate constant for the trimetaphosphate hydration reaction in alkaline medium to the temperature

$T = t + 273°$	$\dfrac{1}{T} \cdot 10^5$	K	$\log K$
1	2	3	4
338	295	0.010	−2.000
348	287	0.022	−1.660
358	280	0.042	−1.370
363	275	0.077	−1.120

Moreover, to confirm the monomolecularity of the hydration reaction, the dependence of the rate constant upon temperature is graphically demonstrated in Fig.2, where the reciprocal of the absolute temperature is indicated on the abscissa axis, and the logarithm of the rate constant on the ordinate axis. The figures required for constructing the graph of temperature dependence of the rate constant, for the hydration reaction of trimetaphosphate in alkaline medium, are cited in Table 6.

The straight line produced indicates that the constants found from experiment are correct, since the points corresponding to their values are well arranged on the straight line.

Using the rate constants for various temperatures, according to the formula $E = \dfrac{RT_1 T_2}{T_2 - T_1} \, 2.303 \log \dfrac{K_2}{K_1}$, the activation energy for the


Fig. 2. Relation of rate constant for the trimetaphosphate hydration reaction in alkaline medium to the temperature

TABLE 7

Hydration of tetrametaphosphate in alkaline medium at a temperature of 75°

Time (in min.)	0.0434 N-KOH (ml)	Normality of the sample solution	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0478	100.0	—
70	4.85	0.0423	88	0.0016
105	4.5	0.0390	82	0.0018
145	4.15	0.0362	76	0.0018
215	4.1	0.0350	73	0.0014
315	3.9	0.0336	70	0.0011
			Average K =	0.0015

TABLE 8

Hydration of tetrametaphosphate in alkaline medium at a temperature of 85°

Time (in min.)	0.0434 N-KOH (ml)	Normality of sample solution	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0478	100.0	—
80	4.40	0.0384	80.5	0.0027
120	3.83	0.0334	69.0	0.0030
220	2.86	0.0248	52.0	0.0029
240	2.75	0.0238	50.0	0.0029
300	2.50	0.0216	45.0	0.0026
			Average K =	0.0029

TABLE 9

Hydration of tetrametaphosphate in alkaline medium at a temperature of 90°

Time (in min.)	0.0584 N-KOH (ml)	Normality of sample solution	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	7.7	0.0900	100	—
55	6.0	0.0705	78	0.0048
85	5.3	0.0601	67	0.0047
140	4.0	0.0464	53	0.0048
180	3.15	0.0370	41	0.0048
			Average K =	0.0048

TABLE 10

Hydration of tetrametaphosphate in alkaline medium at a temperature of 95°

Time (in min.)	0.043 N-KOH (ml)	Normality of sample solution	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0478	100	—
60	3.0	0.0261	55.0	0.010
127	1.5	0.0126	26.5	0.010
187	0.83	0.0072	15.2	0.010
240	0.42	0.0036	7.6	0.010
			Average K =	0.010

TABLE 11

Hydration of tetrametaphosphate in alkaline medium at a temperature of 100°

Time (in min.)	0.0434 N-KOH (ml)	Normality of sample solution	Percentage of remaining phosphate	Rate constant
1	2	3	4	5
0	—	0.0975	100	—
18	8.3	0.0710	73	0.016
60	3.6	0.0410	42	0.015
90	3.1	0.0268	27	0.016
			Average K =	0.016

Fig. 3. Hydration reaction of tetrametaphosphate in alkaline medium. 1. at 75°; 2. at 85°; 3. at 90°; 4. at 95°; 5. at 100°.

trimetaphosphate hydration reaction in alkaline medium was calculated, the average value of which is equal to 20,000 calories.

II. The tetrametaphosphate-ion hydration reaction in alkaline medium was carried out at temperatures of 75, 85, 90, 95 and 100° in a manner similar to that described for the reactions with tremetaphosphate. The alkalinity of the solutions was approximately 0.1 N.

TABLE 12

Half-life periods of the tetrametaphosphate in alkaline medium

Temp (°C)	$\dfrac{\log 2}{K}$	Half-life period in minutes	
		Calculated theoretically	Found by the curves
75	$\dfrac{0.693}{0.0015}$	560	—
85	$\dfrac{0.693}{0.0029}$	240	240
90	$\dfrac{0.693}{0.0048}$	145	143
95	$\dfrac{0.693}{0.010}$	70	80
100	$\dfrac{0.693}{0.016}$	43	43

TABLE 13

Dependence of rate constant for the tetra-metaphosphate hydration reaction in alkaline medium to the temperature

$T = t + 273°$	$\dfrac{1}{T} \cdot 10^5$	K	log K
348	287	0.0015	−2.903
358	279	0.0029	−2.637
363	276	0.0048	−2.320
368	272	0.010	−1.993
373	268	0.0160	−1.793

25 ml of solution was taken for reaction.

Results of the experiments are quoted in tables 7, 8, 9, 10 and 11, and in the curves of Fig. 3, where a curve corresponds to each temperature.

Examination of the monomolecularity of the tetrametaphosphate hydration reaction in alkaline medium has demonstrated a satisfactory conformity of the half-life period values, found graphically by the curves in ig. 3, and calculated theoretically according to the formula $\tau_{1/2} = \dfrac{\log 2}{K}$, the values of which are quoted in Table 12.

In Table 13 are quoted figures for the structure of Fig. 4, showing the relation of the rate constant to temperature.

The resulting straight line indicates that the constants found are accurate, because the points corresponding to their values lie on a straight line.

Utilizing the rate constants found at different temperatures, the activation energy of the tetrametaphosphate hydration reaction in alkaline medium was calculated to be equal, on the average, to 26,000 cal.


Fig. 4. Dependence of rate constant for the tetrametaphosphate hydration reaction in alkaline medium to the temperature.

TABLE 14

Hydration of tetrametaphosphate in acid medium at a temperature of 60°

Time (in min.)	0.0417 N-KOH (ml)	Normality of sample solution	Percentage of remaining m-phosphate	Rate constant
0	10.2	0.0850	100.0	—
25	10.0	0.0834	98.0	0.00093
45	7.8	0.0793	90.0	0.0018
90	8.4 •	0.0695	82.0	0.0018
150	11.8••	0.0654	76.5	0.00178
			Average K =	0.0018

TABLE 15

Hydration of tetrametaphosphate in acid medium at a temperature of 65°

Time (in min.)	0.0474 N-KOH (ml)	Normality of sample solution	Percentage of remaining m-phosphate	Rate constant
0	7.8	0.0740	100	—
25	6.8	0.0645	87	0.0056
100	4.6	0.0438	59	0.0055
165	5.0•••	0.0304	45	0.0054
			Average K =	0.0055
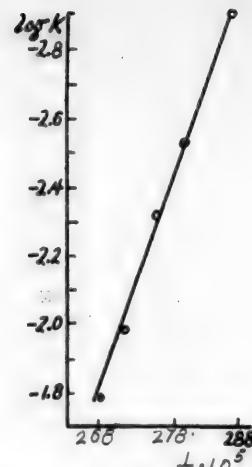
• 10 ml taken for analysis

•• 15 ml taken for analysis

••• 10 ml taken for analysis

TABLE 16

Hydration of tetrametaphosphate in acid medium at a temperature of 75°

Time (in min.)	0.0417 N-NaOH (ml)	Normality of sample solution	Percentage of remaining m-Phosphate	Rate constant
0	9.9	0.105	100	—
10	9.7	0.0940	89.0	0.0115
30	8.7	0.0725	67.5	0.0130
40	7.8	0.0650	62.0	0.0120
55	6.5	0.0523	49.5	0.0120
75	5.5	0.0458	43.5	0.0111
			Average K =	0.012

TABLE 17

Hydration of retrametaphosphate in acid medium at a temperature of 85°

Time (in min.)	0.0417 N-NaOH (ml)	Normality of sample solution	Percentage of remaining m-phosphate	Rate constant
0	10.2	0.0850	100.0	—
20	5	0.0417	49.0	0.035
32	3.3	0.0275	32.4	0.035
50	1.9	0.0158	18.6	0.034
			Average K =	0.034
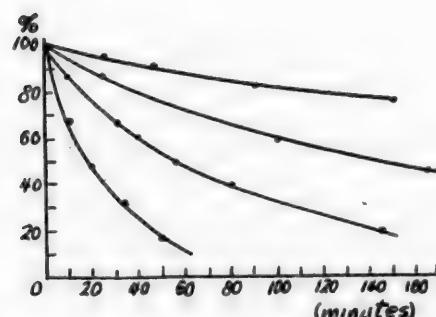
Fig. 5. Hydration reaction of tetrametaphosphate in acid medium

1. at 60°; 2. at 65°; 3. at 75°; 4. at 85°.

TABLE 18

Semidecomposition periods of tetrametaphosphate in acid medium

Temp. (°C)	$\dfrac{\log 2}{K}$	Half-life period (in min.)	
		Calculated theoretically	Found from curves
60	$\dfrac{0.693}{0.0018}$	385	—
65	$\dfrac{0.693}{0.0055}$	128	140.0
75	$\dfrac{0.693}{0.012}$	57.7	57.5
85	$\dfrac{0.693}{0.035}$	19.8	20.0
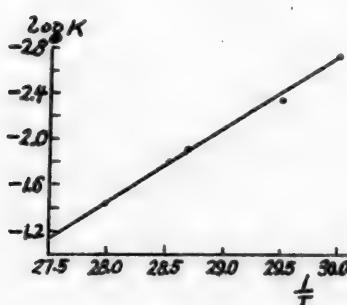

Fig. 6. Dependence of rate constant, for the hydration reaction of tetrametaphosphate in acid medium upon temperature

III. The hydration reaction for the tetrametaphosphate ion in acid medium was carried out in the same manner as described above. The acidity of the medium was approximately 0.15 N. 30 ml of solution was taken for reaction.

Results of the experiments conducted in acid medium, at temperatures of 60, 65, 75 and 85°, are compiled in tables 14, 15, 16, 17, and are graphically represented by the curves in Fig. 5.

TABLE 19

Temperature dependence of rate constant for the hydration reaction of tetrametaphosphate in acid medium

T=t + 273°	$\dfrac{1}{T} \cdot 10^4$	K	log K
358	28.0	0.0018	−1.46
348	28.7	0.0055	−1.92
338	29.5	0.0120	−2.26
333	30.0	0.0340	−2.75

The theoretically calculated half-life periods for tetrametaphosphate-ion in acid medium at various temperatures, which are quoted in Table 18, have shown good agreement with the half-life periods found from the curves of Fig. 5.

To confirm the monomolecularity of the tetrametaphosphate hydration reaction in acid medium, the dependence of the rate constants upon temperature in acid medium has been graphically demonstrated (Fig.6). The numerical data for construction of Fig. 6 are quoted in Table 19.

The activation energy for the hydration reaction of tetrametaphosphate in acid medium was calculated, utilizing the values for the rate constants at various temperatures, according to the formula

$$E = \frac{RT_1 T_2}{T_2 - T_1} \quad 2.303 \log \frac{K_2}{K_1} \, ,$$

the average value for which is 25,300 cal.

SUMMARY

1. In order to confirm the theory of Yu. V. Khodakov about the hydration of phosphoric anhydride and phosphoric acids, the hydration reaction rates for trimeta- and tetrametaphosphate-ions were studied in alkaline and in acid media, at various temperatures, and from the experimental data the rate constants of these reactions were calculated.

For the hydration of trimetaphosphate in alkaline medium the constants are equal to: $K_{65}° = 0.010$; $K_{75}° = 0.022$; $K_{80}° = 0.042$; $K_{90}° = 0.077$.

For the hydration of tetrametaphosphate in alkaline medium the constants are equal to: $K_{75}° = 0.0015$; $K_{85}° = 0.0029$; $K_{80}° = 0.0048$; $K_{90}° = 0.010$; $K_{100}° = 0.016$.

For the hydration of tetrametaphosphate in acid medium the constants are equal to: $K_{80}° = 0.0018$; $K_{65}° = 0.0055$; $K_{75}° = 0.012$; $K_{85}° = 0.034$.

2. The half-life periods of trimeta- and tetrametaphosphates at various temperatures, in acid and in alkaline media, were calculated according to the formula $\tau_{1/2} = \frac{\log 2}{K}$.

3. A comparison of the rate constants, as well as the half-life periods for the trimeta- and the tetrametaphosphates, under the same conditions (t° and pH), confirmed the fact that the trimetaphosphate hydration reaction goes approximately 16 times faster than the tetrametaphosphate hydration reaction.

4. A comparison of the rate constants for the hydration reaction of tetrametaphosphate in alkaline and in acid media has indicated that, in acid medium, the reaction goes approximately 12 times faster than in alkaline medium for the same normality of the solutions.

5. The following were calculated from the experimental data:

1) The activation energy for the trimetaphosphate hydration reaction in alkaline medium: $E = 20,000$ cal.;

2) the activation energy of tetrametaphosphate in alkaline medium: $E = 26,000$ cal.;

3) the activation energy of tetrametaphosphate in acid medium: $E = 25,300$ cal.

6. As a result of the comparison of the activation energy values for the trimeta- and tetrametaphosphate at various pH's, it was determined that the activation energy for the given metaphosphate is approximately of one and the same order.

7. The stable value of the constants for various moments of time indicates that the hydration reactions of the trimeta- and the tetrameta-phosphates, in alkaline as well as acid medium, are found to be of the first order. Moreover, the half-life period of the trimeta- and tetrameta-phosphates does not depend upon the initial concentration, which also confirms the monomolecularity of the hydration reaction for trimeta- and tetrameta-phosphate, both in alkaline and in acid media.

8. The dependence of the hyration reaction rate of trimeta- and tetrameta-phosphates upon temperature was found, which is graphically represented by a straight line.

In conclusion the author wishes to express his great indebtedness to Professor Yu. V. Khodakov for the interesting theme proposed and for the series of valuable directions in the work.

LITERATURE CITED

[1] Yu. V. Khodakov, Proc. Acad. Sci. U.S.S.R., 2, (1944).

[2] Yu. V. Khodakov, Proc. Acad. Sci. U.S.S.R., 5 (1944).

[3] Yu. V. Khodakov and N. I. Rodionova, J. Gen. Chem. 20, No. 8 (1950).*

---

* See Consultants Bureau English translation page 1401

POLAROGRAPHIC ANALYSIS OF CADMIUM IODIDE COMPLEXES

IN WATER–ALCOHOL SOLVENT

A. L. Markman and Ya. I. Turyan

In the preceding paper [1] it was demonstrated that the half-wave potential both of the simple and of the complex ions of cadmium, lead and thallium change in water–alcohol solvent with variation in the alcohol content. A particularly strong displacement of the half-wave potential was observed for cadmium in KI. Simultaneously with increase in ethanol content, the half-wave potential was displaced toward the negative values, which, as was explained by the authors in the same article, is the result of a considerable decrease for the dissociation constant of the complex cadmium ion, in proportion to the addition of alcohol.

The present work is concerned with the determination of the composition of the iodide complexes of cadmium, and their dissociation constants in water–alcohol solvent of varied alcohol content. As far as is known, the given problem has not been discussed at all thoroughly in the literature. It should be noted that in general the effect of the anhydrous solvent upon the composition and the dissociation constant of the complex ion has hardly been studied. At the same time there is no reflection to be cast upon the values of similar investigations from the viewpoint of the theory of solutions and of analytical chemistry.

The authors decided to apply the polarographic method for determining in a given solvent the content of cadmium iodide complexes and their dissociation constants, based upon the reversibility of the reaction of electro-reduction of cadmium at the dropping mercury electrode from water–alcohol solution, which was determined by the authors [1]. The polarographic behavior of cadmium iodide complexes in aqueous solution has been studied in detail by Stromberg and Bykov [2].

EXPERIMENTAL

The iodide complexes of cadmium were investigated in 20, 45 and 65% (by volume) ethanol. The initial solutions contained $1 \cdot 10^{-4}$ M $Cd(NO_3)_2$ and KI; the concentration of the latter was changing from 0.1 to 0.9 M (by 0.2 units). In addition, gelatin (0.01%) was added to all solutions for depression of the maxima. The temperature for the measurements was $25 \pm 0.2°$. The characteristic of the capillary was: $m^{2/3} \tau^{1/6} = 1.50$ mg$^{2/3}$ sec.$^{-1/2}$ (at 0.8-0.9 V, relative to the calomel-saturated electrode). This characteristic was practically independent of the alcohol content in the solution. A more detailed method of experimental procedure is described in the preceding work [1].

The results obtained for cadmium polarography in water–alcohol solvent, with variable concentrations of KI and of alcohol, are represented in Table 1 (diffusion currents) and in Table 2 (half-wave potentials relative to the calomel-saturated electrode).

TABLE 1

Diffusion current in microamperes

C_2H_5OH (%)	Concentration of KI (moles/liter)				
	0.1	0.3	0.5	0.7	0.9
20	5.05	5.02	5.08	5.12	5.08
45	4.09	4.16	4.29	4.32	4.46
65	4.07	4.09	4.22	4.26	4.46

TABLE 2

Half-wave potentials (in V)

C_2H_5OH (%)	Concentration of KI (moles/liter)				
	0.1	0.3	0.5	0.7	0.9
20	−0.647	−0.698	−0.729	−0.747	−0.763
45	−0.673	−0.725	−0.751	−0.764	−0.784
65	−0.705	−0.750	−0.777	−0.794	−0.815

The half-wave potentials were found on the graph (the potential being a function of $\log \frac{i}{i_d - i}$ after corrections were made for the ohm resistance of the electrolyte and for the non-standard potential of the calomel-

saturated electrode [1]. An example of such a graph is represented for 45% alcohol in Figure 1. The angular coefficients of the straight lines (Figure 1) are equal to 0.030 for all concentrations of KI, which attest to the reversibility of the electroreduction process, for the valence of the metallic ion, $\underline{n} = 2$.

Based upon the work of A. L. Brodsky [3], the authors disregarded the very insignificant effect of diffusion potentials upon measurements of the magnitude of the half-wave potentials.

The coordination numbers of the complex ions were found according to the following equation [4]:

$$\frac{d(\pi_{1/2})_C}{d \log C_X f_X} = -p \frac{0.059}{n}, \qquad (1)$$

where $(\pi_{1/2})_C$ is the half-wave potential of the complex ion, C_X and f_X, correspondingly the concentration and the coefficient of the complexing agent activity, $\underline{p}$ is the coordination number of the complex ion, and $\underline{n}$ is the valence of the metallic ion.

It should be noted that derivation of Equation (1) allows: first, invariability of the value of the activity coefficient for the complex ion (f_C) with variation in the concentration of the complexing agent (C_X), which does not correspond to reality, and secondly,

Fig. 1. Determination of the half-wave potential of cadmium in water—alcohol solution of KI. Alcohol concentration 45% (by vol.). KI concentration: 1) 0.1 M; 2) 0.3 M; 3) 0.5 M; 4) 0.7 M; 5) 0.9 M.

invariability of the diffusion current constant (k_C) with variation in the concentration of the complexing agent (C_X), which is occasionally not maintained in practice. For example, in our experiments at alcohol contents of 45% and of 65%, the diffusion current somehow was increasing* with an increase in KI concentration (Table 1), in accordance with the diffusion current constant. Nevertheless, disregarding the minor variations of f_C and k_C with change in C_X in the derivation of Equation (1), the authors do not include the error in determination of the coordination number, $\underline{p}$, as already noted by Stromberg and Bykov [2], since the latter is a whole number, which allows for rounding off the calculation result. For the same reason Kolthof and Lingane [4] recommend, without detriment to the accuracy of the calculation, substitution for the complexing agent activity ($C_X f_X$), the value of the complexing agent concentration (C_X) in Equation (1). In our calculations of the coordination number according to Equation (1), the activity of the complexing agent (KI) in aqueous solution [5] was used instead of the activity of the complexing agent ($C_X f_X$) in water—alcohol solution.

The value of the derivative $\dfrac{d(\pi_{1/2})_C}{d \log C_X f_X}$ in Equation (1) is shown graphically from Figure 2. On the ordinate axis are placed the half-wave potentials ($\pi_{1/2})_C$ (Table 2), and on the abscissa the logarithm of the complexing agent activity. As can be seen from Figure 2, for all three solvents, the sought-for correlation $(\pi_{1/2})_C$ depending upon the log $C_X f_X$ is represented by a straight line, which indicates the stability of the composition of the complex ion within the investigated interval of complexing agent concentration. On the basis of the angular coeffic-

ients of the straight lines $\dfrac{d(\pi_{1/2})_C}{d \log C_X f_X}$ obtained from Figure 2, the corresponding coordination numbers were calculated according to Equation (1), which proved to be the same: the same coordination number is obtained for all solutions; $\underline{p} = 4$,

TABLE 3

Half-wave potentials and the values of diffusion current $1 \cdot 10^{-3}$ M $Cd(NO_3)_2$ in water—alcohol solutions of 0.1 mm NH_4NO_3

C_2H_5OH (%)	$(\pi_{1/2})_s$ (V)	$(i_d)_s$ (cal.)
20	−0.571	4.62
45	−0.560	3.83
65	−0.549	3.53

* Taking into account the above-noted reversibility of the electroreduction process, the variation in diffusion current flow with variation in KI concentration can be explained in the given case by the variability of the diffusion coefficient for the complex ion.

and consequently the composition of the complex ion is: $[CdI_4]^{2-}$. According to the data of Stromberg and Bykov [2], the same composition for the cadmium complex ion was observed in aqueous solutions of KI. Thus, the authors have come to the conclusion that substitution of water for water — alcohol does not affect the composition of cadmium iodide complex.

The calculated constants for the dissociation of the complex ion $[CdI_4]^{2-}$ were derived from the equation quoted from Kolthof an' Lin_ane: [4]:

$$(\pi_{1/2})_C - (\pi_{1/2})_S = \frac{0.059}{n}\log K_C - \frac{0.059}{n}\log\frac{f_s k_C}{f_C k_S} - \frac{0.059}{n}p\log C_x f_x \tag{2}$$

where of the new values: $(\pi_{1/2})_S$ is the half-wave potential of the simple metallic ion; K_C is the dissociation constant for the complex ion; k_C and k_s are the diffusion current constants, respectively, of the complex and of the simple metal ion; f_C and f_S are the activity coefficients, respectively, of the complex and of the simple metal ion.

Fig. 2. Potentials of cadmium half-wave in water—alcohol solution, depending upon the log of the KI activity. 1) 65% CH_2H_5OH; 2) 45% C_2H_5OH; 3) 20% C_2H_5OH.

In the preceding article [1], it was indicated that in water—alcohol solutions of $KNO_3(NH_4NO_3)$ cadmium does not form complex ions with the neutral electrolyte. Thus, polarography of cadmium in given solutions offers the possibility of obtaining values of $(\pi_{1/2})_S$ and k_S, which are essential for calculating the dissociation constant of the complex ion (K_C) according to Equation (2). We have utilized the values obtained by us [1] for 0.1 M NH_4NO_3. Their values are quoted in Table 3 (instead of k_S in Table 3, the proportional k_S values of the diffusion current $(i_d)_S$ are contained). The values $(\pi_{1/2})_C$ and k_C were also taken for 0.1 M KI concentration (Tables 1 and 2). Because of $\frac{k_C}{k_S} = \frac{(i_d)_C}{(i_d)_S}$, then instead of $\frac{k_C}{k_S}$ calculations were made for the diffusion currents $\frac{(i_d)_C}{(i_d)_S}$. The relation of the activity coefficients $\frac{f_S}{f_C}$ was taken as equal to unity, because the charges of both the simple and the complex ions, and also the ionic strengths of the solutions, are the same.

TABLE 4

Dissociation constants of the cadmium complex-ion in water—alcohol solutions of KI

C_2H_5OH (%)	0	20	45	65
K_C	$1.2\cdot10^{-6}$	$0.91\cdot10^{-7}$	$3.3\cdot10^{-9}$	$0.71\cdot10^{-10}$

For calculation of the dissociation constant for the complex ion, the important value, $C_x f_x$, should be calculated as accurately as possible. We did not find in the literature any experimental data on the determination of activity coefficients for KI in water—alcohol solution. The values of these coefficients (f_x) for 0.1 M KI solutions with varied content of alcohol were calculated according to the known formula of Debye-Hückel:

$$\log f_x = -\frac{250\cdot n_i^2\cdot D^{-\frac{3}{2}}\sqrt{I}}{1+2.06\cdot b_i\cdot D^{-\frac{1}{2}}\sqrt{I}}, \qquad \log f_x = \frac{250\cdot n_i^2\cdot D^{-\frac{3}{2}}\sqrt{I}}{1+2.06\cdot b_i\cdot D^{-\frac{1}{2}}\sqrt{I}} \tag{3}$$

which is applicable for moderately concentrated solutions. In this formula $\underline{D}$ is the dielectric constant of the solvent (the value, $\underline{D}$, at various alcohol contents, is quoted in our previous work [1]); b_1 is the constant, which, for KI, as comparison of the calculated and the experimental activity coefficients for KI in aqueous solutions shows, is equal to 5 A; $\underline{I}$ is the ionic strength of the solution; n_i is the ionic valency. After substitution in Equation (2) of the corresponding values $(\pi_{1/2})_C$, $(\pi_{1/2})_S$, $\frac{k_C}{k_S}$, $\underline{p}$, C_x and f_x, the dissociation constants of the complex ions were calculated. The results of these calculations are summarized in Table 4. For aqueous solution, the value K_C was taken from the work of Stromberg and Bykov [2].

As can be seen from Table 4, with an increase in alcohol content there occurs a sharp decrease in the dissociation constant of the complex ion $[CdI_4]^{2-}$. Thus, for 65% alcohol, the dissociation constant is approximately 10-20 thousand times smaller than the dissociation constant in aqueous solution. It is evident that the observed decrease in dissociation constant for the complex ion is first of all correlated with a decrease in the dielectric constant of the solvent. Additional work in this direction should make it possible to determine the qualitative relationship between the dissociation constant and the dielectric constant of the solvent.

SUMMARY

1. A polarographic determination of the composition of the cadmium iodide complexes and their dissociation constants in water—alcohol solutions of KI, with varied alcohol content, was carried out.

2. It was demonstrated that the coordination number of the complex ion does not change with change in alcohol content, but remains the same as in aqueous solutions.

3. It was demonstrated that the dissociation constant of the complex ion decreases sharply with an increase in alcohol concentration.

LITERATURE CITED

[1] A.L. Markman and Ya. L. Turyan. J. Gen. Chem., 22, 1715 (1952); see Consultants Bureau translation, p. 1757.

[2] A.G. Stromberg and I.E. Bykov. J. Gen. Chem., 245 (1949); see Consultants Bureau translation, p. 209.

[3] A.I. Brodsky. Survey of the Thermodynamics and Electrochemistry of Solutions. Technical edition, page 170, 435 (1931).

[4] Kolthoff and Lingane, Polarography. Russ. ed. State Chemical Press, p. 169 (1948).

[5] Landolt Börnstein. Phys. Chem. Tab. Erg., Bd. III (1936).

# FORMATION OF BASIC AND ACID BISMUTH CITRATES UPON THERMAL DECOMPOSITION OF AMMONIUM CITROBISMUTHATE

N. M. Turkevich

The simplest bismuth citrate $C_6H_5O_7Bi \cdot H_2O$ exhibits acid properties and forms complex salts with alkali which are soluble in water. Many authors [1-4] have studied its structure, and have most frequently ascribed to it a formula with one or two carboxyl groups (I), (II), (III), (IV):
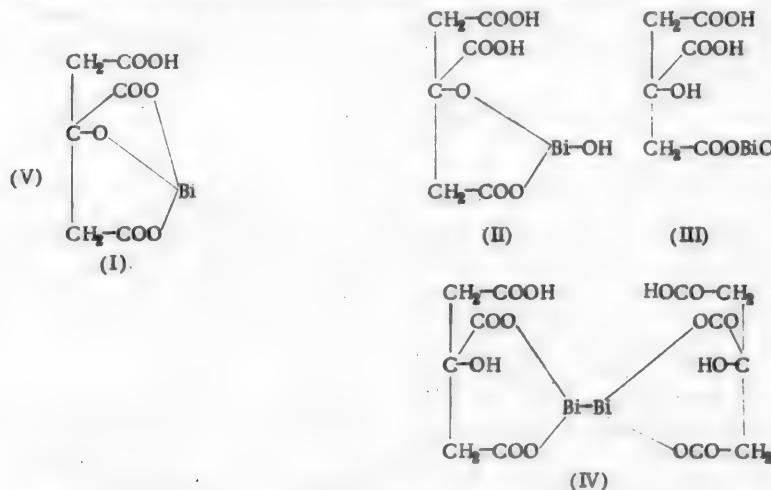
On the basis of certain properties (the presence of coordinately-bound water which passes off very slowly, even at 105°, the easy replacement of this water by ammonia molecules with the formation of ammoniate, and others) the author [5] assigns the structure of aquo compound (V) to bismuth citrate — abbreviated as $CiBi \cdot OH_2$, where Ci denotes the citric acid residue. Bismuth citrate forms [6], upon solution in ammonia, a salt of the general formula $(3NH_4OH \cdot 2BiCi \cdot 3H_2O)_n$, soluble in water without hydrolysis. The determination of the number $\underline{n}$ with
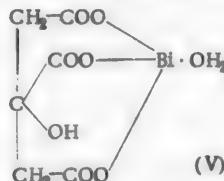
the help of the molecular weight is difficult because ammonium citrobismuthate does not dissolve in organic solvents, and, in water, is exposed not only to electrolytic dissociation, but also to partial depolymerization (to the point of monomers — as regards the number of bismuth atoms in the ion). Deduction can be made, on the assumption of various transformations of ammonium citrobismuthate, that $\underline{n}$ is equal to a minimum of 2, and thus, for simplicity, we shall use for it the formula of the tetramer $6NH_3 \cdot 4BiCi \cdot 12H_2O$.

The monomeric ammonium salt of the structure $(CiBi \cdot OH)NH_4$, the anhydride of which the author [6] has isolated in the form of an ammoniate, $CiBi \cdot NH_3$, has not been described up to the present time. There appear in the literature short notices about the three basic or acid citrates. Bismutho-dicitric acid $BiCi \cdot CiH_3 \cdot xH_2O$ is obtained [7] by reaction of citric acid with bismuth nitrate in glycerine medium. The basic citrate — $BiCi \cdot 4Bi(OH)_3$, is obtained [8] by heating an ammoniacal solution of $BiCi$, and the salt $Ci(BiO)_2Na$ is formed [4] by dissolving $BiCi$ in a solution of NaOH.

The author has found that upon heating ammonium citrobismuthate, not only is water expelled, but also ammonia, and different acidic and basic salts are formed. While boiling with benzene, 6 molecules of water are expelled and an insignificant amount of ammonia, with the formation of $6NH_3 \cdot 4BiCi \cdot 6H_2O$. Further heating of the sample dehydrated in this way at 105° leads to gradual loss of the ammonia molecule. 1 mole of ammonia is volatilized within 9 hours, but the product $5NH_3 \cdot 4BiCi \cdot 6H_2O$ remains soluble in water, and 1 more mole of ammonia and 1 mole of water are volatilized during 32 hours, forming a water-insoluble substance $4NH_3 \cdot 4BiCi \cdot 5H_2O$. From the aqueous solution $5NH_3 \cdot 4BiCi \cdot 6H_2O$ barium chloride precipitates monomeric barium citrobismuthate $Ba(CiBi \cdot OH)_2 \cdot 5H_2O$. The substance $4NH_3 \cdot 4BiCi \cdot 5H_2O$ hydrolyzes easily in water and alkali. Upon reaction with water, there occurs formation of basic bismuth citrate and the ammonium salt of acid bismuth citrate, according to the equation:

$$4NH_3 \cdot 4BiCi \cdot 5H_2O \longrightarrow BiCi \cdot BiOOH + NH_4OH \cdot (NH_4)_3Ci \cdot 2BiCi \cdot 2H_2O.$$

Dibismuth-monocitrate $BiCi \cdot BiOOH$ (or structurally: $HO \cdot Bi = Ci-BiO$) is entirely devoid of acid properties. With the ammonium and potassium citrates it forms water-soluble complex salts. From an aqueous solution of the ammonium salt $[NH_4]_2Ci-Bi = Ci-Bi[OH]-Ci[NH_4]_2$, representing the salt of dibismuth-tricitrate, alcohol precipitates the monomeric ammonium salt:

$$NH_4OH \cdot (NH_4)_3Ci \cdot 2BiCi \cdot 2H_2O \longrightarrow 2NH_4(CiBi \cdot OH) \cdot H_2O + (NH_4)_2HCi,$$

difficultly soluble in water.

The initial ammonium citrobismuthate, when heated at 50°, loses 2 moles of water, and upon further heating at 80° (for 12 hours) five more moles of water, and only an insignificant amount of ammonia. Subsequent heating of the sample at 105° (for 24 hours) leads to volatilization of 3 more moles of water and to 3 moles of ammonia, with the formation of a water-insoluble product of the abbreviated formula $3NH_3 \cdot 4BiCi \cdot 2H_2O$. The basic citrate and the ammonium salt are formed upon water hydrolysis, according to the equation:

$$3NH_3 \cdot 4BiCi \cdot 2H_2O + 2H_2O \longrightarrow 2BiCi \cdot BiOOH + (NH_4)_3Ci \cdot BiCi \cdot H_2O.$$

It follows from a comparison of the formulas that the two substances obtained are the salts of the simplest acid bismuth citrate $BiCi \cdot CiH_3$, i.e. the bismutho-dicitric acid (structurally: $H_3Ci-Bi = CiH$). The dibismuth salt of bismutho-dicitric acid $HO \cdot Bi = Ci-Bi = Ci-BiO$ is entirely devoid of acid properties. Its very great solubility in solutions of Seignette's salt excludes the possibility of the presence of bismuth hydroxide, or the ammoniate of bismuth citrate, in the form of impurities. The ammonium salt of bismutho-dicitric acid can be represented structurally by the abbreviation: $(NH_4)_3Ci-Bi = CiNH_4$.

Further heating of ammonium citrobismuthate at 130° leads to volatilization of 1 more mole of ammonia. Upon hydrolysis of the obtained product by water, there is obtained more than 88% dibismuth salt of bismutho-dicitric acid.

The basic bismuth citrates (dibismuth-monocitrate and tribismuth-dicitrate) are obtained by thermal decomposition of ammonium citrobismuthate; they possess a high degree of purity, and only in rare cases is contamination by ammoniates (up to 0.4% N).

EXPERIMENTAL

Elimination of 1 Mole of Ammonia from Ammonium Citrobismuthate. 10 g of ammonium citrobismuthate was boiled with benzene for 18 hours, and the volume of water distilled off was determined by a volumetric procedure, according to the method of Diene and Stark. The volume of water measured − 0.54 ml −corresponded to the loss of 6 moles of H_2O (5.4% water instead of the theoretical 5.66%).

303.4 mg substance: 9.9 ml 0.1 N HCl. Found %: N 4.57. $6NH_3 \cdot 4BiCi \cdot 6H_2O$. Calculated %: N 4.66.

The dehydrated substance was soluble in water and in ammonia solutions. 12 g of the dehydrated sample was further heated for 9 hours at 105° to the elimination of 1 mole of ammonia. The heating time was determined in a preliminary way on a small quantity of the sample. A slight yellowing of the sample was observed during the process.

266.8 mg substance: 7.2 ml 0.1 N HCl. Found %: N 3.78. $5NH_3 \cdot 4BiCi \cdot 6H_2O$. Calculated %: N 3.92.

Barium Citrobismuthate. 9.38 g of the latter sample was mixed with 100 ml of water and then heated to boiling. The sample dissolved almost completely, but very slowly. The insoluble sediment (0.12 g − 1.3%) was

centrifuged off and washed with water, and it represented (on the basis of analysis and properties) the basic bismuth citrate $OBi-Ci=Bi OH$. 100 ml of 10% barium chloride solution was added to the filtrate, heated to boiling. After being allowed to stand, the white insoluble precipitate was centrifuged off, and washed with water to the disappearance of a chloride reaction. After washing with alcohol, the sample was air-dried.

227.7 mg substance: 40.9 mg CO_2; 111.1 mg H_2O. 200.5 mg substance: 43.8 mg $BaSO_4$; 115.0 mg $BiPO_4$. Found %: C 13.32; H 2.01; Bi 39.44; Ba 12.86. $C_{12}H_{22}O_{21}Bi_2Ba$. Calculated %: C 13.62; H 2.10; Bi 39.52; Ba 12.99.

Monomeric barium citrobismuthate appeared to be a microcrystalline substance, insoluble in water, alcohol and ether, and soluble in an ammoniacal solution of ammonium citrate. In ammonia it underwent hydrolysis.

Elimination of 2 Moles of Ammonia from Ammonium Citrobismuthate. Ammonium citrobismuthate, dehydrated, dehydrated by boiling in benzene, was heated for 32 hours at 105°. The substance after 12 hours of heating acquired a light yellow-green color. The product obtained was insoluble in water and soluble in ammonia and in ammoniacal solution of ammonium citrate.

408.4 mg substance: 8.4 ml 0.1 N HCl. 267.4 mg substance: 142.6 mg Bi_2O_3. Found %: N 2.88; Bi 47.83. $4NH_3 \cdot 4BiCl \cdot 5H_2O$. Calculated %: N 3.20; Bi 47.76
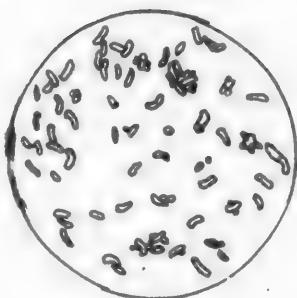

Fig. 1. Monomeric ammonium citrobismuthate X 678.

Dibismuth-monocitrate and the Ammonium Salt of Dibismuth-tricitrate. 8.8 g of the preceding product was finely ground in a mortar with water and was mixed for half an hour with 250 ml of water. After 24 hours of standing the mixture was filtered, and the white precipitate obtained was washed with water, alcohol, and dried at 105°. 3.3 g of the water-insoluble, microcrystalline basic bismuth citrate BiCi · BiOOH was obtained. The sample was insoluble in ammonia, but soluble in an ammoniacal solution of ammonium citrate.

187.4 mg substance: 136.8 mg Bi_2O_3. 54.3 mg substance: 22.3 mg CO_2; 5.3 mg H_2O. Found %: Bi 65.48; C 11.20; H 1.09 $C_6H_4O_9Bi_2$. Calculated %: Bi 65.30; C 11.26; H 0.95.

The aqueous solution was steamed off on a water bath after filtration of the basic bismuth citrate, and dried at 105° (for 6 hours).

199.9 mg substance: 7.2 ml 0.1 N HCl. 185.9 mg substance: 77.9 mg Bi_2O_3. Found %: N 5.05; Bi 37.69. $NH_4OH \cdot (NH_4)_3C \cdot 2BiC \cdot 2H_2O$ Calculated %: N 5.05; Bi 37.63.

Ammonium Monohydroxycitrobismuthate. Four times the quantity of alcohol was added to a 2% aqueous solution of ammonium dibismuth-tricitrate. After a month and a half of standing, the precipitate was centrifuged off, washed with alcohol and dried at room temperature in a vacuum desiccator. The white substance obtained (Figure 1) was very difficultly soluble in water, but soluble in an ammoniacal solution of ammonium citrate. The sample dissolved in ammonia, but hydrolysis occurred upon heating

58.3 mg substance: 33.4 mg CO_2; 14.5 mg H_2O. 145.7 mg substance: 3.4 ml 0.1 N HCl. 120.6 mg substance: 61.2 mg Bi_2O_3. Found %: C 15.63; H 2.78; N 3.27; Bi 45.52. $(C_6H_5O_7Bi \cdot OH)NH_4 \cdot 1.5H_2O$. Calculated %: C 15.66; H 2.85; N 3.04; Bi 45.42

Elimination of 3 Moles of Ammonia from Ammonium Citrobismuthate. 3.3637 g of ammonium citrobismuthate was dried at 50°. After 10 hours of drying, the weight was practically unchanged. Loss in weight was 59.9 mg, which corresponds to 1.9 moles of water. Upon further heating at 80°, the loss in weight ceased almost completely after 12 hours, corresponding to 5 moles of water.

558.7 mg substance: 16.9 ml 0.1 N HCl. Found %: N 4.24. $6NH_3 \cdot 4BiCl \cdot 5H_2O$. Calculated %: N 4.71.

Additional heating was conducted at 105°. After two hours, loss in weight became insignificant. The results of heating at 50, 80 and 105° are represented in Fig. 2.
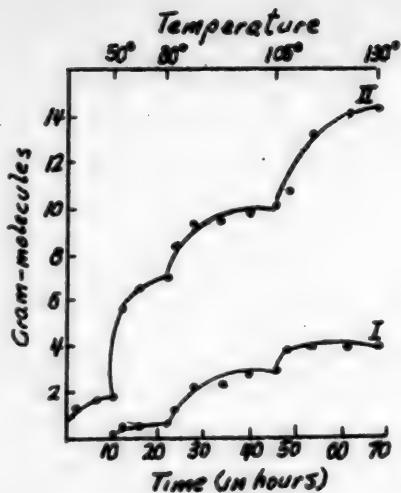
Fig. 2. Heating of Ammonium Citrobismuthate.
I) volatilization of ammonia, II) volatilization of water.
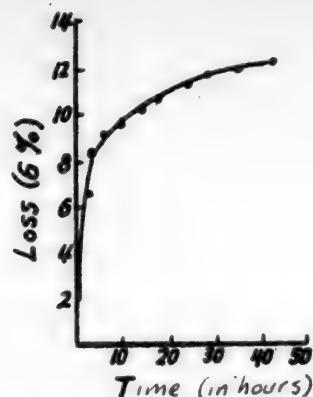
Fig. 3. Heating of ammonium citrobismuthate at 105°

279.7 mg substance: 4.9 ml 0.1 N HCl.
Found %: N 2.46. $3NH_3 \cdot 4BiCi \cdot 2H_2O$.
Calculated %: N 2.50.

The product obtained had a light yellow shade, insoluble in water, soluble in ammonia and in ammoniacal solution of ammonium citrate.

An identical product was obtained upon direct heating of original ammonium citrobismuthate at 105° for 42 hours (Figure 3).

521.4 mg substance: 9.7 ml 0.1 N HCl. Found %: N 2.61. $3NH_3 \cdot 4BiCi \cdot 2H_2O$. Calculated %: N 2.50.

Dibismuth and Ammonium Salts of Bismutho-dicitric Acid. 330.0 mg of the preceding sample was mixed with 100 ml of water for half an hour. After standing 48 hours, the precipitate was filtered off, washed thoroughly with water and dried at 105°. 59.9% of the dibismuth salt of $2BiCi \cdot BiOOH$ was obtained (instead of the theoretically calculated 61.2%), in the form of a white, microcrystalline sample, insoluble in water and lacking in acid properties. The sample was insoluble in ammonia but soluble in an ammoniacal solution of bismuth citrate.

84.5 mg substance: 57.0 mg Bi_2O_3. 66.2 mg substance: 32.8 mg CO_2; 7.1 mg H_2O. Found %: Bi 60.51; C 13.52; H 1.20. $C_{12}H_{11}O_{16}Bi_3$. Calculated %: Bi 60.39; C 13.88; H 1.07.

The aqueous solution was steamed off on the water bath after filtration of the dibismuth salt and dried at 105° (4 hours)

19.9 mg substance: 0.9 ml 0.1 N HCl. 26.5 mg substance: 9.4 mg Bi_2O_3. Found %: N 6.34; Bi 31.81. $(NH_4)_2Ci \cdot BiCi \cdot H_2O$. Calculated %: N 6.37; Bi 31.70.

Further heating of the sample $3NH_3 \cdot 4BiCi \cdot 2H_2O$ at 130° (22 hours; see Figure 2) leads to the formation of a brown product, containing 1 less mole of ammonia (with an overall loss in weight of 19.45%).

202.0 mg substance: 2.25 ml 0.1 N HCl. Found %: N 1.56.

Upon treatment of the product with water, followed by thorough washing, there was obtained 88.17% of basic bismuth citrate $2BiCi \cdot BiOOH$ in the form of an almost white product.

SUMMARY

1. Changes in the composition of ammonium bismuth citrate upon heating at 50, 80, 105 and 130°, and upon boiling in benzene, were studied.

2. Two basic bismuth citrates ($BiCi \cdot BiOOH$ and $2BiCi \cdot BiOOH$), were obtained, the ammonium salts of two acid bismuth citrates ($BiCi \cdot CiH_3 \cdot H_2O$ and $2BiCi \cdot CiH_3 \cdot 2H_2O$) and ammonium and barium citrobismuthates

Ba(CiBi · OH)$_2$ and NH$_4$(CiBi · OH), where Ci denotes the citric acid residue.

LITERATURE CITED

[1] M. Picon, J. Pharm. Chem. (8), 5, 62 (1927).

[2] Fabregue, Th. Ph. Sup. Montpellier (1925).

[3] W. F. Oettingen, Y. Ishikawa, T. Sollman, J. Pharm. exp. Ther. 31, 353 (1927).

[4] F. W. Adams, Pharm. J. 113, 87 (1924).

[5] N. M. Turkevich, Ukrainian Chem. J. 15, 244 (1949).

[6] N. M. Turkevich, Ukrainian Chem. J. 15, 248 (1949).

[7] P. Godfrin, J. Pharm. Chem. (8), 6, 49 (1927).

[8] Cavazzi, Gazz. 14,289 (1884).

ACTIVE CARRIERS DURING HYDROGENATION

D. V. Sokolsky

Catalytic hydrogenation requires activation on the surface of the catalyst of both the hydrogen and of the hydrogenated compound. Naturally, the most favorable conditions for activation of the separate components may not coincide and an increase in temperature almost always changes not only the speed of the primary reaction, but also the relative concentrations of the reacting substances on the catalyst surface. As a result, there is observed a negative temperature coefficient above 40° [1] when a majority of organic compounds are hydrogenated in the presence of elementary nickel catalyst. By activating, or inactivating, the catalyst, it is possible to increase or to decrease the activation of one of the reacting components. Thus, for example, when Pt, Pd or Rh is deposited upon nickel catalyst, the hydrogen is almost always principally activated, whereas Os, Ru and Re actually lower the activity of nickel catalyst. At room temperature osmium black displays activity upon hydrogenation of the double bond, the carbonyl group and the nitro group [2], during which time the hydrogenation proceeds stepwise. Under these conditions, acetylenic hydrocarbons do not fully hydrogenate, which is explained by the competition between the hydrogen and the acetylene group on one and the same sections of the catalyst. During hydrogenation on Pt, Pd or Ni, both the adsorbed and the dissolved hydrogen take part in reaction. To a lesser extent the question of activation of the unsaturated component during reaction has been studied. In this case it may be expected that the structural correspondence between catalyst and reacting molecule will be of primary importance. An assumption has been made that superficially completely inactive osmium and ruthenium blacks actually activate the double bond and active hydrogen is lacking only on their surface. Following deposition on their surfaces of palladium or of platinum, which activate hydrogen particularly well, the potential possibilities of such "active carriers" should be manifested and it should be possible to obtain highly active catalysts. This assumption was fully confirmed, using the hydrogenation of dimethylacetylenylcarbinol.

EXPERIMENTAL

(With the assistance of N. Sinaiskaya and M. Zakharova)

The hydrogenation was studied in 96% ethanol solution under conditions described earlier [3]. For catalysts were used: Pt, deposited on $BaSO_4$, or on $BaSO_4$ coated first with Os, and also by Pd on $BaSO_4$ coated with ruthenium. The active carriers were prepared according to the method of N. D. Zelinsky [4], calculated in such amount as to obtain a 20% Os or Ru content on $BaSO_4$. The "active carriers" were dried at room temperature in a dessicator over H_2SO_4. Their characteristic activity was examined by hydrogenation of nitro benzene and was found to be equal to zero. Part of the $Os-BaSO_4$ and $Ru-BaSO_4$ was reduced at 200° for 4 hours and subsequently remained inactive. A weighed portion of "active carrier", equal to 2 g, was transferred to a flask with the aid of 15 ml of alcohol; there was also introduced, by a pipet, a defined volume of chlorplatinate or of palladium chloride solution. The flask was shaken for 30 minutes, for better adsorption of the promoter, and the catalyst was further saturated with hydrogen for 30 minutes at 25°. After saturation, there was placed in the flask a defined weight of dimethylacetylenylcarbinol and 10 ml of alcohol was added. The system was washed rapidly with hydrogen, the motor switched on and readings on absorbed hydrogen started.

Hydrogenation of Dimethylacetylenylcarbinol on Catalysts $Pt-BaSO_4$ and $Pd-BaSO_4$. It was found that the hydrogenation rates of the double and of the triple bond on Pt and Pd deposited on $BaSO_4$ differed. In Fig.1 is represented a series of kinetic curves for the hydrogenation of dimethylacetylenylcarbinol on $Pt-BaSO_4$ catalyst. One peculiarity is characteristic for all curves − the reaction rate remains almost stationary up to the absorption of approximately 70-75% of the calculated volume of hydrogen and then increases sharply.

It may be assumed that on the first horizontal segment, linkage of one hydrogen molecule to the triple bond occurs, and simultaneously partial hydrogenation of the ethylene derivative produced starts. As soon as hydrogenation of the triple bond is terminated, the double bond starts to hydrogenate with much greater speed. To examine this assumption, the experiments were interrupted at the moment when the increase in reaction rate started. The products of incomplete hydrogenation were poured off rapidly from the catalyst and tested for the presence of hydrogen at the triple bond by the use of ammoniacal silver nitrate; in all cases the absence of the acetylenic alcohol was established.
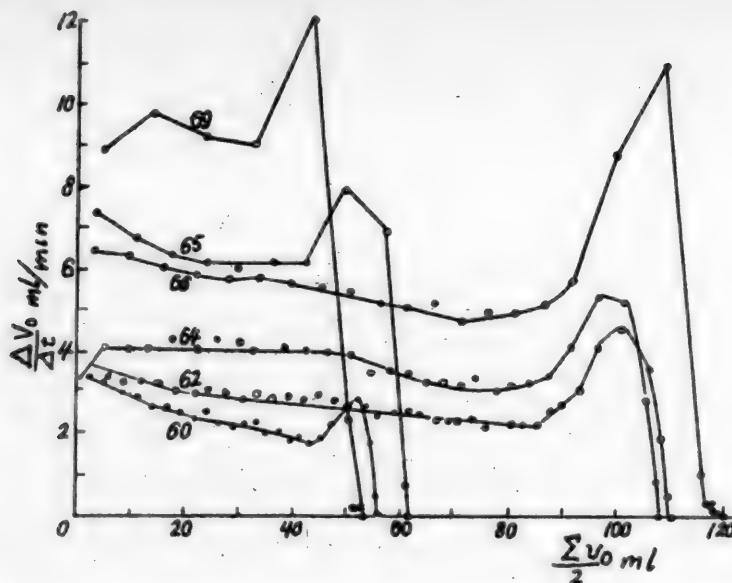
Fig. 1. Hydrogenation of Dimethylacetylenylcarbinol on Pt–BaSO$_4$ Catalyst.
(BaSO$_4$ 0.2 g, ethyl alcohol 25 ml).

Expt. No.	Quantity of Pt (g)	Temperature	Quantity of Carbinol (ml)
60	0.00103	25°	0.12
62	0.00103	25	0.24
64	0.00103	40	0.24
65	0.00206	25	0.13
66	0.00206	25	0.26
69	0.00206	40	0.12

It is known that Pt dissolves very little hydrogen and, furthermore, under our conditions, the Pt atoms either form very fine crystals or penetrate into the incomplete lattice work of the carrier; thus adsorbed hydrogen plays the principal role in hydrogenation. Compounds with a triple bond adsorb very well on the surface of the platinum metal group, and, in addition, they are activated on the centers, that are similar to the centers which activate the hydrogen.[1]. As a result of this competition, the speed of hydrogenation of the triple bond on platinum catalysts is usually smaller than the speed of hydrogenation of the double bond. In the absence of compounds with a triple bond, the hydrogen concentration on the surface increases. In complete accordance with this view, as the curves of Fig. 1 indicate, the hydrogenation speed of the triple bond decreases with the dimethylacetylenylcarbinol increase in concentration and the hydrogenation speed of the double bond increases.

For characterization of curves of a similar type, we are introducing the value, a, representing the relation between the maximum speed of hydrogenation to the average speed of hydrogenation of the triple bond (the first segment of the curve). The value, a, as experiments indicate, depends very little upon the activity of the catalyst, upon the quantity of Pt deposited upon BaSO$_4$, or upon the temperature. Thus, in a whole series of experiments with 0.12 ml of dimethylacetylenylcarbinol, upon a change in quantity of Pt from 0.00103 to 0.00412 g, and a temperature from 25 to 40°, the relation of speeds a changed only from 1.1 to 1.3, i.e., within the range of experimental error. Contrariwise, the value a, is very sensitive to concentration change, and under the same conditions, with 0.24 ml of dimethylacetylenylcarbinol, fluctuated from 1.7 to 2.2.

It should be noted that with an increase in temperature the hydrogenation speeds of the triple and the double bond increase, but the former rises more rapidly and the relation of the speed a decreases somewhat. This phenomenon is quite understandable if one assumes that, with temperature rise under the conditions involved, the speed of the primary reaction increases and general adsorption decreases.
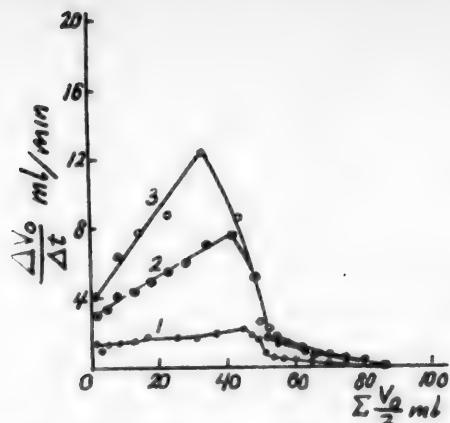
Fig. 2. Hydrogenation of Dimethylacetylenylcarbinol on catalyst Pd—BaSO$_4$. (BaSO$_4$ 0.2 g., Pd 0.00012 g, ethyl alcohol 25 ml).

Expt. No.	Temperature
1	1°
2	25
3	40

TABLE 1

Added Pt (g)	Carbinol taken (ml)	Temperature	a average
0.00051	0.12	25°	4.20
	0.24	25	4.70
	0.12	40	3.85
0.00103	0.12	25	2.63
	0.12	40	2.50
	0.24	40	4.30
0.00206	0.12	25	1.95
	0.24	25	3.00

In Fig. 2 is represented a series of curves on another catalyst, Pd—BaSO$_4$. In this case the correlation of speeds is entirely different; the reaction speed in the first half of the process is considerably greater than in the second and consequently the triple bond hydrogenates more rapidly than the double bond. Selectivity of the catalyst in this case is considerably greater and the break in the speed, corresponding to a loss of a triple bond in the compound, is observed after absorption of 55-68% of the calculated quantity of hydrogen (reaction with ammoniacal AgNO$_3$). A similar course of the curves in the presence of Pd, which is similar in lattice structure to that of Pt, can be related only to the participation of dissolved hydrogen in the reaction. It is known that Pd dissolves hydrogen readily and that this hydrogen takes part in the reaction, as we have shown earlier [3]. In this instance the hydrogen and the acetylene derivative activation are basically related to the different surface sections, or more correctly, with the mass of the catalyst. The gradual increase in speed during the first half of the process can be related to the increased role of adsorbed hydrogen by the rate of concentration decrease of the compound with the triple bond. Thus, in the case of palladium catalyst, it is impossible to limit oneself to examination of the role of dissolved hydrogen only. It is necessary to take into account the gradual increase in role of the adsorbed hydrogen. The variable correlation of hydrogenation speeds of the triple and double bonds in the presence of Pt and Pd on BaSO$_4$ made it of particular interest to study the effect of Os and Ru as a coater from the point of view of clarifying this correlation.

As has already been mentioned, Os and Ru on BaSO$_4$ were found to be entirely inactive in the hydrogenation reaction. Both metals have the hexagonal lattice with parameters: Os a 2.7244 A, with 4.3044 A , Ru a 2.695 A, with 4.273 A , and can, from structural considerations, at low temperature, only result in activation of the double bond by a given amount of hydrogen and not the triple bond.

Hydrogenation of Dimethylacetylenylcarbinol on catalyst Pt—[Os—BaSO$_4$]. A series of curves is represented in Fig. 8, which were obtained in the presence of Os. The shape of the curve remains the same under all conditions, and is similar to the curves obtained in the absence of Os. However, the hydrogenation speed of the triple bond is almost unchanged and the hydrogenation speed of the double bond increases sharply. As a result, the value, a, increases also. Thus, the presence of Os can be considered to be catalyzing only in relation to the second part of the process, i.e., to the hydrogenation of dimethylvinylcarbinol. Upon increase in concentration of the dimethyl- acetylenylcarbinol, the hydrogenation speed of the triple bond decreases and the hydrogenation speed of the double bond increases (curves for Experiments 5 and 6, 9 and 10, 30 and 31, 16 and 17).

The deductions made become more graphic when the average values for "a" (Table 1) are calculated.

As can be seen from Fig. 3 and from the data of Table 1 during the small steps in the filling of the platinum surface, an acceleration in double bond hydrogenation is noticed.

Fig. 3. Hydrogenation of dimethylacetylenylcarbinol on catalyst Pt—[Os—BaSO$_4$]. (Os—BaSO$_4$ 0.2 g, ethyl alcohol 25 ml).

Expt. No.	Pt Quantity (g)	Temperature	Carbinol quantity (ml)
4	0.00103	25°	0.12
5	0.00103	25	0.12
6	0.00103	25	0.24
9	0.00051	25	0.12
10	0.00051	25	0.24
30	0.00103	40	0.12
31	0.00103	40	0.24
16	0.00206	25	0.12
17	0.00206	25	0.24

For a given quantity of Pt during the greatest changes in activity of the catalyst the correlation of the hydrogenation speeds, a, is almost unchanged. The same regularities were found by the author upon subsequent filling up of the Os—BaSO$_4$ surface by platinum, beginning with from 0.00021 to 0.00165 g of Pt for 0.2 g of "active carrier". Pt on Os—BaSO$_4$ was found to be a very stable catalyst and it is possible to conduct more than 10 experiments on the one sample without noticeable lowering of the activity.

Similar series of experiments were carried out with Pt, deposited on Os—BaSO$_4$, previously reduced at 200°. It is necessary to note that the catalyst in this case is even more stable and active. A very interesting phenomenon was observed after prolonged work with one and the same weighed sample of reduced catalyst: the activity of the catalyst decreased from experiment to experiment and the relation of the hydrogenation speeds of the double and the triple bonds, a, increased. This experimental result can be explained by the fact that the Pt atoms are able in time to penetrate deeply into the crystalline lattice of the Os—BaSO$_4$ carrier, as the result of which "a" increases.

Hydrogenation of dimethylacetylenylcarbinol on catalyst Pd—[Ru—BaSO$_4$]. The kinetic hydrogenation curves are represented in Figs. 4, 5, 6. The triple bond hydrogenates in this case considerably more rapidly than the double bond. Comparative data on hydrogenation in the presence of, and in the absence of, Ru are given in Table 2 for the two series of experiments.

TABLE 2

| Series and catalyst	Expt. No.	Temp.	Carbinol t'aken (ml)	Maximum speed (ml/min.)	K for hydrogenation of double bond	Duration of hydrogenation (in min.)	
						of the triple bond	of the double bond
VIII BaSO$_4$ + 0.00036 g Pd	29	25°	0.2	26.5	0.87	2	22
	30	40	0.2	38.7	1.60	1	14
IX Ru–BaSO$_4$ + 0.00036 g Pd	32	25	0.2	30.0	2.15	2	7
	33	25	0.2	30.5	1.88	2	7
	35	40	0.2	48.3	3.73	1	6
	36	40	0.4	51.1	4.01	2	7
	37	40	0.6	50.7	4.01	3	10
	34	25	0.2	28.0	–	2	8
	31	1	0.2	10.0	0.44	5	27
	38	25	0.2	25.5	1.88	2	9
	39	25	0.4	26.7	1.80	4	13
After 72 hours of standing for the catalyst	40	1	0.4	7.4	0.28	15	45
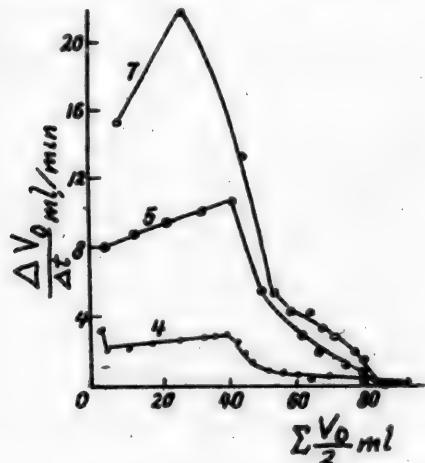
Fig. 4. Hydrogenation of d imethylacetylenyl-carbinol on catalyst Pd–[Ru–BaSO$_4$]. (Ru–BaSO$_4$ 0.2 g Pd 0.00012 g, ethyl alcohol 25 ml).

Expt. No.	Temperature
4	1°
5	25
7	40

TABLE 3

Temp. interval	Catalyst			
	Pd–BaSO$_4$		Pd–[Ru–BaSO$_4$]	
	E of triple bond hydrogenation (cal/mol)	E of double bond hydrogenation (cal/mol)	E of triple bond hydrogenation (cal/mol)	E of double bond hydrogenation (cal/mol)
1–25°	8–9000	7–8000	7–8000	8–9000
25–40	4–5000	6–7000	5–6000	6–7000

As can be seen from the data of Table 2 and the curves of the graphs, the average speed of hydrogenation in the presence of Ru at all temperatures is considerably higher. However, the hydrogenation time of the triple bond, in the presence of Ru, is the same as without it, while the hydrogenation time of the double bond in the presence of Ru decreases from 22 to 7 minutes, i.e., more than threefold. The relation of hydrogenation speed $\dfrac{K(Ru)}{K(without\ Ru)}$ constitutes: at 25°, 2.3; at 40°, 2.33; of maximum speed at 25°, 1.18; at 40°, 1.25. In all other series of experiments the hydrogenation speed of the double bond also increases more rapidly than the hydrogenation speed of the triple bond. The presence of Ru starts to become noticeable at elevated temperature (40°), evidently, as the result, the activation of the unsaturated bonds over Ru is hampered by low temperature. As can be seen from the data of Table 1 and of Fig. 6, the maximum hydrogenation speed is almost independent of the concentration of dimethylacetylenylcarbinol in solution. The catalyst Pd–[Ru–BaSO$_4$] is very stable and all experiments of the series were carried out with one catalyst. It should be noted that with an increase in the quantity of palladium at a constant quantity of Ru, the effect of the latter begins to weaken and the catalyst approaches that of the catalyst Pd–BaSO$_4$.

Fig. 5. Hydrogenation of dimethylacetylenylcarbinol with catalyst Pd–[Ru–BaSO$_4$].
(Pd 0.00024 g)

Expt. No.	Temperature	Carbinol quantity (ml)
14	25°	0.1
15,16,17,18	25	0.2
20	40	0.2

Upon deposition of 0.00048 g of Pd, the difference in the properties of the catalysts with Ru becomes evident only at high temperature. The activation energies for the hydrogenation of the triple bond and of the double bond are found on the basis of 13 series of experiments to be variable for catalysts with and without Ru (Table 3).

The activation energy for the triple bond and for the double bond hydrogenation is considerably higher in the temperature interval 1–25° than in the interval 25–40° as can be seen from the data of Table 3.

At the elevated temperatures the ability of the unsaturated compound to extract dissolved hydrogen from the catalyst increases and along with it the quantity of hydrogen adsorbed on the surface is decreased. The conjugation of the two factors augments the role of dissolved hydrogen, of which diffusion there is naturally a small temperature coefficient. In almost all cases the activation energy for hydrogenation of the triple bond was found to be lower than that for the double bond.
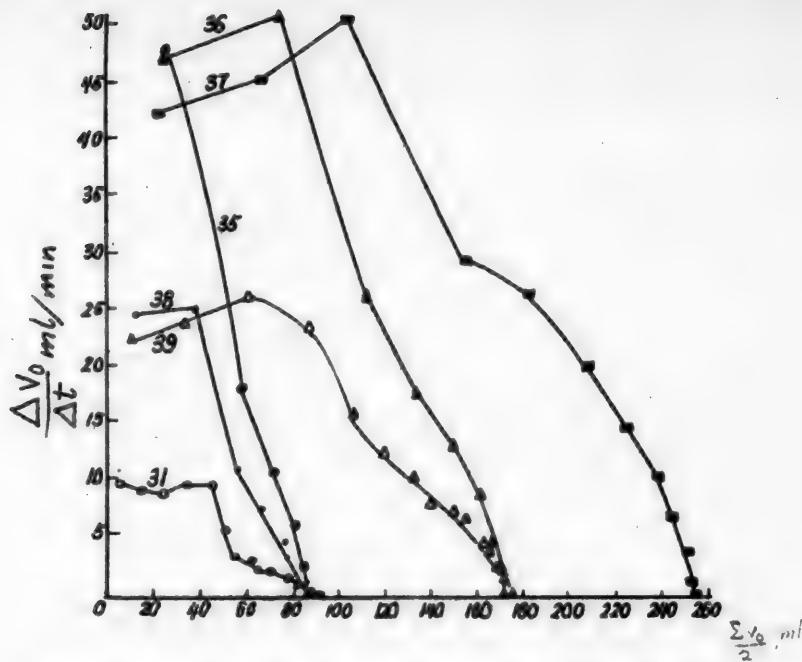
Fig. 6. Hydrogenation of dimethylacetylenylcarbinol with Pd – [Ru – BaSO₄].
(Pd 0.00036 g).

Expt. No.	Temperature	Carbinol quantity (ml)
31	1°	0.2
38	25	0.2
39	25	0.4
35	40	0.2
36	40	0.4
37	40	0.6

SUMMARY

The results obtained by the author indicate the necessity for examining separately the effect of carrier upon the behavior of hydrogen and the hydrogenated compound in hydrogenation reactions. In the case of hydrogenation of dimethylacetylenylcarbinol, Os and Ru, on BaSO₄, were found to be the carriers which first of all activate the double bond, regardless of the fact that there is an entirely opposite correlation for hydrogenation speeds for the double and the triple bond, which is conditioned by variable percentage participation in reaction of the dissolved and the adsorbed hydrogen upon Pt and Pd. The different effects of substituents on the hydrogenation speed upon Pt and Pd were also demonstrated by B. A. Kazansky and G. T. Tatevosyan [5]. In the case examined, the structural correlation between the molecule and the catalyst enters into the foreground.

The problem of structural correlation acquires now particular actuality in the light of discussion on the "theory of resonance" and it seems somewhat strange that some authors recently have been prepared to reject entirely this principle in organic catalysis. It is inevitable, no doubt, to reject certain complex elements of symmetry, postulated by the multiple theory and hardly realizable from the point of view of no less obligatory energy correlation.

In the case given, the problem of energy correlation is presented only in the sense of a distinction in the

role of adsorbed and dissolved hydrogen. Potentiometric measurements demonstrate that the catalyst potential falls rapidly when compounds with a triple bond are hydrogenated on Pt, regardless of how small the speed of reaction is; during the transition to double bond hydrogenation, the reaction rate and the potential both increase sharply at the same time.

The increase in the amount of hydrogen at the surface with the increase in reaction rate can only be connected with the fact that in the presence of acetylene derivatives, hydrogen desorbs from the surface and passes off into the gaseous state.

The quantity of hydrogen which can be diluted in 0.00048 g of Pd (maximum quantity) is quite insufficient for hydrogenation and evidently there occurs incessantly in the course of the reaction, replenishment of the dissolved hydrogen. Hydrogen on Os and Ru activates only with great difficulty and predominantly at increased temperatures. In this manner some decrease of a with increase in temperature can be explained.

LITERATURE CITED

[1] D.V. Sokolsky. Problems of Kinetics and Catalysis, VI. Heterogeneous Catalysts, 157 (1949).

[2] D.V. Sokolsky and A.I. Vyugova. Scientific Reports of the Kazakh University, 13, 83 (1951).

[3] D.V. Sokolsky and A.B. Bukhman. Reports of the Academy of Science of the Kazakh SSR, Chemical Series, 64 (1948).

[4] N.D. Zelinsky and M.B. Turova-Polyak, See N.D. Zelinsky, Selected Works, Vol. 2, 1958 (1941).

[5] B.A. Kazansky and G.T. Tatevosyan. J. Gen. Chem., 9, 2248, 2256 (1939).

THE INTERACTION OF ISOPROPYLMAGNESIUM BROMIDE WITH THE ETHYL ESTER OF FORMIC ACID AND WITH THE CHLORANHYDRIDE OF ISOVALERIC ACID

E.B.Sokolova

Upon the interaction of secondary and tertiary alkylmagnesium halides with carboxylic acid esters, and also with the chloranhydrides and the salts of acids, there takes place the formation of ketones of the type $RCOR_1$ and $RCOR$, where $\underline{R}$ is an acid radical and R_1 is an alkyl halide radical.

The character of the reaction products formed is determined by the properties of both the alkyl halide and of the acid entering into reaction. The effect of the nature of the Grignard reagent radical and the nature of the acid entering into the composition of the ester, or chloranhydride, in the case of syntheses involving the use of tertiary alkyl halides, has been studied in the many works of A.D.Petrov and coworkers [1], I.I.Lapkin [2], and others [3]. These works demonstrated the influence upon the course of the Grignard synthesis of different compound radicals as regards spatial interferences and chemical activity entering into reaction.

The purpose of the present work was a study of the interactions of secondary alkyl halides with ethers and with chloranhydrides under conditions of synthesis according to Grignard with the examples of isopropyl bromide on the one hand and of the ethyl ester of formic acid and the chloranhydride of isovaleric on the other.

The results of the work carried out demonstrated that in the case of interaction of isopropylmagnesium bromide with ethyl formate, reaction occurs only in the normal fashion and results in the formation of the secondary alcohol diisopropylcarbinol, with a yield of about 40%. The interaction of this ester with tertiary-butylmagnesium chloride leads to the formation of tertiary-butylcarbinol (an abnormal reaction product), according to the data of Favorsky and Kolotova [4].

In the case of interaction of isopropylmagnesium bromide with the chloranhydride of isovaleric acid, reaction occurs according to the normal scheme, in contrast to interaction of isovaleric acid derivatives with tertiary-butylmagnesium chloride [5], but is complicated by a side reaction of reducible character. The reaction occurs principally in the direction of the secondary alcohol, isopropylisobutylcarbinol — the reduction product of the ketone, type $RCOR_1$ and the ester — the esterification product of this alcohol with isovaleric acid.

EXPERIMENTAL

1. Reaction of isopropylmagnesium bromide with the ethyl ester of formic acid. For reaction there were taken: 160 g (1.3 mole) of the alkyl halide with b.p. 59-60°, 29 g (1.2 g-atom) of magnesium shavings, and 45 g (0.6 mole) of the ester with a b.p. of 54°. The reaction was carried out in the usual manner, the ester being added to the Grignard reagent. The secondary alcohol —diisopropyl carbinol, to the amount of 28 g, was separated from the reaction products which constituted about 40% of the theoretical yield, on the basis of ester taken for the synthesis. The structure of the derived alcohol was proved by its oxidation to the corresponding ketone, from which was prepared the semicarbazone, with a m.p. of 157° An attempt to find among the reaction products a combination of the type $RCOR_1$ and its corresponding reduction product (in the case of formic acid and isopropylbromide, the presence of isobutyric acid and isobutyl alcohol) was unsuccessful.

2. Reaction of isopropylmagnesium bromide with the chloranhydride of isovaleric acid. For reaction were taken: 210 g (1.7 mole) of isopropyl bromide, 38.5 g (1.6 g-atom) of magnesium shavings and 97 g (0.8 mole) freshly distilled chloranhydride of isovaleric acid. After removal of ester, the reaction product was distilled off from a Favorsky flask in 5-degree fractions. The maximum yield of product corresponded to a b.p. of 150-155° (12.9 g) and at 155-160° (12.0 g). Anticipating the presence of the secondary alcohol — isopropylisobutylcarbinol — in these fractions formed by reduction of the ketone, $RCOR_1$, the normal reaction product, we conducted the following tests: 1) percent determination of hydroxyl group in the fraction with the b.p. of 155-160° (corresponding to isopropylisobutylcarbinol, boiling in the range of 156-158° according to the literature data) and 2) oxidation of the 155-160° fraction and test on the oxidation product for the ketone group.

Determination of the percent hydroxyl group in the 155-160° b.p. fraction according to the method of Verley, indicated the presence of 9.1% of OH group, which corresponds to an alcohol content in the fraction of about 70% of the composition $C_3H_7CHOHC_4H_9$.

A separate sample of the fraction with b.p. 155-160° was oxidized by chromic acid mixture. Upon treatment of the oxidation products with semicarbazide a copious precipitate of crystalline derivative, with a m.p. of 143°, was obtained. (According to the literature data, the semicarbazone of isopropylisobutylketone melts at 142°).

3.39 mg substance: 0.683 ml N_2 (22°, 746 mm). 3.14 mg substance: 0.629 ml N_2 (22°, 746 mm). Found %: N 22.88, 22.79. $C_9H_{19}ON_3$. Calculated %: N 22.7.

The fractions with b.p. 140-145° and 145-150° were combined and tested for the presence of ketone of the type $RCOR_1$. As a result of the treatment of the fraction with semicarbazide a semicarbazone precipitated, with a m.p. of 143°. A sample mixed with the semicarbazone of isopropylisobutylketone did not give a depression.

An attempt to obtain the semicarbazone of a ketone of the type RCOR from the fraction with b.p. 160-170° gave negative results.

The fraction with a b.p. of 220-230°, obtained by distilling off the reaction products in significant quantity (7.4 g), was analyzed for ester content. Elementary analysis showed, from the C and H content, that the product examined comes very near to the ester of isovaleric acid and the isopropylisobutylcarbinol of the composition $C_4H_9COOC_8H_{17}$.

5.67 mg substance: 15.14 mg CO_2; 5.84 mg H_2O. 4.70 mg substance: 12.58 mg CO_2; 4.89 mg H_2O. Found %: C 72.82, 73.00; H 11.52, 11.64. $C_{13}H_{26}O_2$. Calculated %: C 72.9; H 12.1.

A few grams of the fraction with b.p. 220-230° was saponified with 15% alcoholic alkali (KOH) for several hours. The saponification products were examined for the presence of alcohol and acid. The oily layer, which floated up after dilution of the saponification products with water, was separated, washed with water, dried and distilled. The temperature of the product obtained was within the limits 153-163°. Identity of the obtained product with that of the alcohol — isopropylisobutylcarbinol — was proved by its oxidation to the corresponding ketone, from which was obtained the semicarbazone with m.p. 142°. A mixed sample did not show melting point depression.

The water—alcohol layer of the saponification products was acidified with nitric acid after removal of the alcohol and the organic acid was then precipitated in the form of its silver salt.

0.6048 g substance: 0.3148 g Ag. Found %: Ag 52.05. C_4H_9COOAg. Calculated %: Ag 51.67.

SUMMARY

1. It was demonstrated that the secondary alcohol — diisopropylcarbinol — is obtained in 40% yield by interaction of isopropylmagnesium bromide with ethylformate.

2. In the case of interaction between isopropylmagnesium bromide and the chloranhydride of isovaleric acid, the reaction goes in the direction, principally, of the formation of secondary alcohol, isopropylisobutylcarbinol, which is the product from the reduction of the ketone, $RCOR_1$, and of the ester which is the product of esterification of this alcohol with isovaleric acid.

LITERATURE CITED

[1] A.D.Petrov, K.I.Karasev and M.A.Cheltsova. J.Gen.Chem., 6, 522 (1936); A.D.Petrov and M.S.Malinovsky. J.Gen.Chem., 7, 565 (1937); A.D.Petrov and E.B.Sokolova. J.Gen.Chem., 8, 199 (1938); A.D.Petrov and P.S. Sanin. J.Gen.Chem., 8, 195 (1938); 9, 2199 (1939); A.D.Petrov and N.A.Roslova. J.Gen.Chem., 10, 973 (1940).

[2] I.I.Lapkin. J.Gen.Chem., 16, 721 (1946); 17, 1939 (1947).

[3] V.I.Egorova. J.Russ.Phys.Chem.Soc., 41, 1454 (1909); E.D.Venus. J.Russ.Phys.Chem.Soc., 46, 1332 (1914); Fr.Whitmore and D.Badertscher. J.Am.Chem.Soc., 55, 1559 (1933); F.Greenwood, Fr.Whitmore, and H.Crooks. J.Am. Chem.Soc., 60, 2028 (1938); Fr.Whitmore and T.Heyd. J.Am.Chem.Soc., 60, 2030 (1938).

[4] A.E.Favorsky and L.I.Kolotova. J.Russ.Phys.Chem.Soc., 38, 759 (1906).

[5] A.D.Petrov and M.S.Malinovsky. J.Gen.Chem., 7, 565 (1937).

SELECTIVE MALONIC SYNTHESIS

V. P. Golmov

The malonic synthesis, involving dihaloid derivatives, has not yet been studied in sufficient detail. As is known, the reaction proceeds mainly in three directions upon interaction of sodium malonic ester with dihaloid derivatives and forms the following mixture of products:

$$(I) \quad X(CH_2)_nX + NaCH(COOC_2H_5)_2 \rightarrow X(CH_2)_nCH(COOC_2H_5)_2.$$

$$(II) \quad X(CH_2)_nCH(COOC_2H_5)_2 + NaCH(COOC_2H_5)_2 \rightarrow (C_2H_5OCO)_2CH(CH_2)_nCH(COOC_2H_5)_2.$$

$$(III) \quad X(CH_2)_nCH(COOC_2H_5)_2 \rightarrow (CH_2)_nC(COOC_2H_5)_2.$$
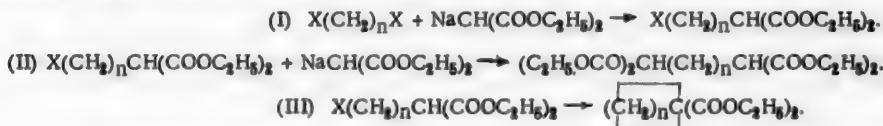
Up to the present time, a reaction of the type given was conducted primarily for the purpose of obtaining the esters of cyclic or of polybasic acids. There are comparatively few known works, the purpose for which was found to be the derivation of intermediately-formed esters of the halogen-substituted alkylmalonic acids; thus the conditions for the formation of these substances, and also their reactions, have received little study.

The following haloidsubstituted monoalkylmalonic esters are described in the literature: 1) β-chlorethylmalonic ester, obtained by N. Ya. Demyanov and V. V. Feofilaktov [1] through the addition of HCl to cyclopropane-1,1-cyanocarboxylic ester in the presence of alcohol; 2) β-bromethylmalonic ester [2], obtained by addition of HBr to cyclopropane-1,1-dicarboxylic ester; 3) γ-chlorpropylmalonic ester [3]; 4) γ-brompropylmalonic ester [4]; 5) γ-iodopropylmalonic ester [5], resulting from interaction of sodium malonic ester with 3-chlor-1-brompropane, 1,3-dibrompropane and 3-chlor-1-iodopropane; 6) γ-chlorisobutylmalonic ester, obtained by B. A. Kazansky and M. Yu. Lukina [6] from sodium malonic ester and 3-chlor-1-brom-2-methylpropane; 7) δ-chlorbutylmalonic ester [26], resulting from sodium malonic ester and 4-chlor-1-brombutane; 8) ζ-iodhexylmalonic ester, obtained by V. P. Golmov [7] from sodium malonic ester and hexamethylene iodide; 9) β-bromoctylmalonic ester [27], resulting from addition of brommalonic ester to octene-1, and, finally, 10) κ-bromdecylmalonic ester [8], derived from sodium malonic ester and decamethylene bromide. Upon the interaction of equimolecular quantities of sodium malonic ester and a dihaloid derivative containing two atoms of one and the same halogen, the corresponding haloidsubstituted alkylmalonic ester results in negligible yield.

The author of the present article has demonstrated [9] that γ-brompropylmalonic ester can be obtained with a yield 70% of theory if there can be removed at the same time the side reactions of formation of the ester of cyclobutane-1,1-dicarboxylic acid and also the ester of pentane-1,1,5,5-tetracarboxylic acid (reactions II and III). Reaction (III) can be retarded by using a large excess of malonic ester, whose presence in the reaction mixture shifts reversible reaction (IV) to the left:

$$IV. \quad BrCH_2CH_2CH_2CH(COOC_2H_5)_2 + NaCH(COOC_2H_5)_2 \rightleftarrows BrCH_2CH_2CH_2CNa(COOC_2H_5)_2 + CH_2(COOC_2H_5)_2.$$

and decreases the concentration of sodium-γ-brompropylmalonic ester, and consequently the cyclization speed of the latter.

Reaction (II) can also be suppressed to a considerable degree if a large excess of trimethylene bromide is used, together with the excess of malonic ester, in accordance with the law of mass action. Similar results were obtained by the author [7] upon reaction of hexamethylene iodide with sodium malonic ester, and by Ziegler [8] upon reaction of decamethylene bromide with the latter.

In the present work we have tried first of all to explain to what extent the given procedure is applicable for obtaining haloidsubstituted alkylmalonic esters with other alkyl radicals. For this purpose, we have reacted sodium malonic ester with a series of dihaloid derivatives, the atoms of which halogen are located in positions 1,2; 1,3; 1,4 and 1,5 to each other.

The results of these, and also of earlier described experiments [7,8,9], led to the following conclusions. Upon reacting sodium malonic ester with 1,3; 1,5 and 1,6 dihaloid derivatives with unbranched chain, the corresponding haloid-substituted alkylmalonic esters are formed in good yields, the amount of which is determined by the excess of dihaloid derivative. It can be calculated, beforehand, what yield of haloid-substituted alkylmalonic ester will be obtained in each individual case, upon applying a given excess of dihaloid derivative.

This calculation is based upon the following theoretical considerations. The speeds of reactions (I) and (II) are expressed by the following equations:

$$\frac{dx}{dt} = k_1(a-x)(b-x-y), \tag{I}$$

$$\frac{dy}{dt} = k_2(x-y)(b-x-y), \tag{II}$$

where: a and b = initial concentrations of the dihaloid derivative and the sodium malonic ester, and x and y = the concentrations of the products of reactions (I) and (II) formed in time t. If k_1 is taken to be equal to k_2, which is quite justifiable experimentally, as can be seen from the data of table 1, then from the equations for the reaction rates is obtained:

$$\frac{dy}{dx} = \frac{x-y}{a-x} \tag{III}$$

Integrating equation (III), there is found:

$$x-y = 2.3(a-x)\log\frac{a}{a-x} \tag{IV}$$

Taking $x + y$ as 100%, the yield of haloidsubstituted alkylmalonic ester $(x-y)$ can be calculated. In Table 1 the calculated results are compared with the yields, obtained experimentally at various values for a.

Upon reaction of sodium malonic ester with 1,4-dibromoderivatives, by the application of as much as 4 times the quantity of malonic ester as against theory it is still not possible to decrease to any considerable degree the cyclization of δ-bromalkylmalonic ester and thus the principal reaction product is found to be in this case the compound with a five-membered ring for the molecule and the δ-bromalkylmalonic ester is formed in yield only 3-5% of the theoretical. The reason for such poor yield is apparently the large constant for rate of formation of the five-membered ring; thus, even with a negligible concentration of the sodium derivative of δ-bromalkylmalonic ester in the reaction mixture, the reaction is directed principally in the direction of formation of the compound with a five membered ring, which results in a yield about 75% of the theoretical. This assumption is in agreement with the data in Table 3 of the present work and also with the experiments of Freundlich and Solomon [24] which had to do with measuring the rate constant for the formation of various cyclic imines. The results of their measurements demonstrate that the rate constant for the formation of the five-membered ring is approximately 800 times greater than that of three-membered and 70 times larger than of the six-membered ring. Bennett and co-workers [25], examining the relative ease of cyclization of β- and δ-chlorsulfites, have also found that the rate constant for the formation of the five-membered ring is 76 times greater than that of the six-membered.

TABLE 1

Substance	haloidalkylmalonic ester yield (in %)		
	a = 100%	a = 200%	a = 400%
BrCH$_2$CH$_2$CH$_2$CH(COOC$_2$H$_5$)$_2$	36.0	—	70.3
ICH$_2$CH$_2$CH$_2$CH(COOC$_2$H$_5$)$_2$	41.4	58.0	—
BrCH$_2$(CH$_2$)$_3$CH$_2$CH(COOC$_2$H$_5$)$_2$	40.9	60.4	—
ICH$_2$(CH$_2$)$_4$CH$_2$CH(COOC$_2$H$_5$)$_2$	33.8	51.9	—
BrCH$_2$(CH$_2$)$_4$CH$_2$CH(COOC$_2$H$_5$)$_2$	—	64.4	—
Average	38.0	58.7	70.3
Calculated by formula (IV)	36.6	60.6	78.4

The same low yields of intermediate products are obtained upon interaction of sodium malonic ester with 1,2-dihaloid derivatives. The authors were not able to obtain the β-bromethylmalonic ester by reacting sodium malonic ester with ethylene bromide- when ethylene chloride was used, the resulting β-chlorethylmalonic ester resulted in yield of only 8% of theory. The principal reaction product in both cases is cyclopropane-1,1-dicarboxylic ester. The reason for such a peculiar course of action is not clear. It is apparently not possible to assume that the results obtained are conditioned by the large rate constant for formation of the three-membered ring, because cyclopropane-1,1-dicarboxylic ester results from β-bromethyl malonic ester, according to the data of Kuster and Grassner [2] with a poorer

yield than, for example, cyclobutane-1,1-dicarboxylic ester from γ-brompropylmalonic ester [10] (Table 3); however, under the same conditions, the latter results in a yield of 70% of theory [9].

Thus, the results of our experiments demonstrate that to obtain β- or δ-haloidalkylmalonic esters by the use of malonic ester, it is disadvantageous to proceed from the symmetrical dihaloid derivatives. For derivation of δ-bromalkyl malonic esters, a second method described below can be employed, namely the addition of hydrogen bromide to the alkenylmalonic esters. As is known, the γ-brompropylmalonic ester was obtained by this procedure from allylmalonic ester [10], and also α-bromdihydrocinnamylidenemalonic ester from cinnamylidene ester [11]. In the present work we have synthesized a new alkenylmalonic ester by reacting sodium malonic ester with 5-bromhexene-1, namely α-methyl-δ-pentenylmalonic ester $CH_2\!=\!\!CHCH_2CH_2CH(CH_3)CH(COOC_2H_5)_2$. Upon addition of HBr to it in ether solution, α-brom-δ-methylamylmalonic ester results in the form of a stereoisomeric mixture, the structure of which was proven by its method of cyclization, at which time there resulted a mixture of stereoisomeric 2,5-dimethylcyclopentane-1,1-dicarboxylic esters, described earlier by Wislicenous [12] and also by Jacobs and Florsheim [13].

ϵ-iodamylmalonic ester was also obtained by reacting sodium iodide with ϵ-bromamylmalonic ester.

In Table 2 the physical properties of the haloidsubstituted alkylmalonic esters obtained by us are compiled.

TABLE 2

Substance	Boiling point	d_4^{20}	n_D^{20}
$ClCH_2CH_2CH(COOC_2H_5)_2$	122-123° (3 mm)	1.1300/17°	1.4425/17°
$ClCH_2CH_2CH_2CH(COOC_2H_5)_2$ [3]	136° (5mm)	1.1010/21°	1.4434/21°
$BrCH_2CH_2CH_2CH(COOC_2H_5)_2$	132-134° (4 mm)	1.2834	1.4590
$BrCH_2(CH_2)_2CH_2CH(COOC_2H_5)_2$	133-136° (2 mm)	1.2567	1.4594
$BrCH_2(CH_2)_3CH_2CH(COOC_2H_5)_2$	143-144° (1.5mm)	1.2310	1.4609
$CH_3CHBrCH_2CH_2CHCH(COOC_2H_5)_2$ * $\quad CH_3$	145-147° (2 mm)	1.2054	1.4605
$CH_3CHBrCH_2CH_2CHCH(COOC_2H_5)_2$ ** $\quad CH_3$	143-144° (2 mm)	1.2075	1.4616
$ICH_2CH_2CH_2CH(COOC_2H_5)_2$	138° (1.5 mm)	1.4601	1.4869
$ICH_2(CH_2)_3CH_2CH(COOC_2H_5)_2$	162° (3 mm)	1.3808	1.4844
$ICH_2(CH_2)_4CH_2CH(COOC_2H_5)_2$ [7]	168° (2 mm)	1.3433	1.4839

Having obtained the above-described haloid-substituted alkylmalonic esters, we have utilized them to solve the question of the relative ease of formation of the smaller polymethylene rings under the conditions of malonic synthesis. This question cannot be regarded as fully clarified up to the present, because in the preceding works based upon a given course, wherein derivation of cyclic esters was conducted without isolation of the intermediate products [14, 15, 16] it is impossible to make proper deductions, because of the side reactions which distort the true picture of cyclization.

Certain polymethylene-1,1-dicarboxylic esters have already been earlier derived from haloidsubstituted alkylmalonic esters. Thus, V. P. Golmov and B. A. Kazansky [3] obtained cyclobutane-1,1-dicarboxylic ester from γ-chlorpropylmalonic ester by reaction of the latter with sodium alcoholate. Wibaut and coworkers [17] have obtained the same ester by reacting solid caustic potash with γ-brompropylmalonic ester. The cyclization of γ-chlorisobutylmalonic ester was also accomplished, with the aid of sodium alcoholate, by B. A. Kazansky and M. Yu. Lukina [6], of γ-brompropylmalonic ester by Walborsky [10], of β-bromethylmalonic ester by Kuster and Grassner [2], and of ζ-iodhexylmalonic ester by V.P. Galmov [7]. The results of these works demonstrate that three- and four-membered rings are formed with ease and in good yields, with the help of the method given. On the other hand, it was found that seven-membered rings are formed with more difficulty under these conditions than the others.

In the present work, the above-mentioned data are supplemented by information on the relative ease of formation of compounds with five- and six-membered rings from δ- and ϵ-haloidalkylmalonic esters. In view of the fact that δ-brombutylmalonic ester was not obtained in quantity sufficient for the purpose of experimentation with five-membered rings, it was necessary that we limit ourselves to the cyclization of only δ-brom-α-methylamylmalonic ester.

For comparison, γ-iodpropyl- and ϵ-iodamylmalonic ester were also subjected to cyclization, at which time it was found that the nature of the halogen has little effect upon the yield of cyclic product. Finally, in view of the fact that concentration of γ-brompropylmalonic ester, described earlier [10], was carried out in

* From meso-2,5-dibromhexane and sodium malonic ester

** From α-methyl-δ-pentenylmalonic ester

considerably diluted solution we have repeated these experiments in solution of high concentration. The data obtained, which characterize the relative ease with which different rings are formed, by the malonic synthesis, are compiled in Table 3.

TABLE 3

Ring	Yield of cyclic esters (in %)		Ring	Yields of cyclic esters (in %)	
	From bromester	From iodester		From bromester	From iodester
△	64.5	–	⬠	87.2	–
▢	71.7	70.0	⬡	60.1	61.6
				–	3.0

δ-Brombutylmalonic Ester

The tetramethylene bromide required for the experiment given was obtained by the method of Marvel and Tannenbaum [18]. Modifications consisted, first of all, in obtaining the ester of γ-phenoxybutyric acid which is sensitive to reduction, not from the nitrile of γ-phenoxybutyric acid, as did the above-cited authors, but rather by the esterification of γ-phenoxybutyric acid, which was prepared from sodium malonic ester and β-bromphenetole [19,20]; secondly, for the reduction of the ester of γ-phenoxybutyric acid, the author applied the method of Prins [21], through which the δ-phenoxybutyl alcohol is obtained more conveniently than in absolute alcohol medium.

Reduction of γ-Phenoxybutyric Acid Ester. 35 g of γ-phenoxybutyric acid ester, dissolved in 100 ml of sulfuric ether, was placed in a flask equipped with mechanical stirrer and dropping funnel, and containing 50 ml of a saturated solution of sodium acetate. 22 g of metallic sodium was gradually added at a temperature of from -5° to -2°, with slow mixing, and simultaneously, 30% acetic acid dropwise. After completion of reaction, water was added until the precipitated salt dissolved, the upper layer was separated, and the lower was extracted once with ether. The ether solution was dried with anhydrous potash, the ether distilled off, and the residue distilled in vacuo, upon which the δ-phenoxybutyl alcohol boiled in the range 145-150° at 10-12 mm. It was in the form of a colorless, oily liquid, which solidified into a crystalline mass upon standing. Yield on the average was 17 g or 60% of theoretical.

The tetramethylene bromide derived from the δ-phenoxybutyl alcohol upon reaction of the latter with hydrogen bromide and sulfuric acid mixture [18], boiled at 69° (7 mm); d_4^{17} 1.8131; n_D^{17} 1.5203.

Reaction of Sodium Malonic Ester with Tetramethylene Bromide. 5.75 g (0.25 g-atom) of metallic sodium was dissolved in 75 ml of absolute alcohol, and 160 g (1 mole) of malonic ester then added, followed by 54 g (0.25 mole) of tetramethylene bromide. The mixture was heated to boiling on a bath for 2 hours, and the reaction then became neutral. After cooling, water was then added, the reaction products were extracted with ether, the ether extraction washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue fractionated in vacuo, during which time three fractions resulted: 1) b.p. up to 84° (mainly 69-74°) at 4 mm - 165 g; 2) b.p. 84-92° at 3 mm - 23 g; 3) b.p. 135-138° at 3 mm - 2.7 g Negligible residue remained in the flask after boiling as above.

The 84-92° fraction, upon repeated distillation, boiled mostly at 83° (3 mm) and represented cyclopentane-1,1-dicarboxylic ester (yield 86%); d_4^{20} 1.0490; n_D^{20} 1.4435; MR_D 54.02; calculated 54.11.

The 135-138° fractions, combined from the experiments, after repeated distillation in vacuo boiled at 133-136° at 2 mm, and judging from the constants and the analysis results, represented impure δ-brombutylmalonic ester (yield 3.6% of theoretical); d_4^{20} 1.2567; n_D^{20} 1.4594; MR_D 64.22; calculated 64.07.

0.2243 g substance; 0.3705 g CO_2; 0.1347 g H_2O; 0.4337 g substance: 0.2670 g AgBr. Found %: C 45.06. H 6.67; Br 26.22. $C_{11}H_{19}O_4Br$ Calculated %: C 44.75; H 6.44; Br 27.12.

δ-Brom-α-methylmalonic Ester

6.9 g (0.3 g-atom) of metallic sodium was dissolved in 75 ml of absolute alcohol. 192 g (1.2 mole) of malonic ester was added to the alcoholate solution, and then 73.2 g (0.3 mole) of meso-2,5-dibromhexane, m.p. 38-39°, obtained by addition of hydrogen bromide to 5-bromhexene-1. The mixture was heated on a bath to boiling for 6 hours, and then, after cooling, was diluted with water, acidified with sulfuric acid, the reaction

products extracted with ether, the ether extract ı washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue fractionated ın vacuo. During this time the following fractions resulted: 1) b.p. up to 78° at 2 mm (mixture of malonic ester with 2,5-dibromhexane) - 205g; 2) b.p. 100-108° at 4 mm - 18.3 g; 3) b.p. 145-147° at 2 mm - 5.4 g. A negligible residue remained in the flask.

The 100-108° fraction, upon repeated distillation in vacuo, boiled mainly at 90-91° (1.5 mm) and was found to be the ester of cis-2,5-dimethylcyclopentane-1,1-dicarboxylic acid. 9.7 g of the latter acid was saponified by alcholic KOH, the alcohol distilled off, the residue diluted with water and acidified with sulfuric acid. During this time there was precipitated 7.7 g (90% of theory) of crystalline substance, which boiled at 81° after recrystallization from aqueous formic acid [13], and represented the acid ester of cis-2,5-dimethylcyclopentane-1,1-dicarboxylic acid.

The 145-147° fraction was found to be impure ester of δ-brom-a-methylamylmalonic acid (yield 5.6 % of theoretica·l); d_4^{20} 1.2054; n_D^{20} 1.4605; MR_D 73.39; calculated 73.31.

0.1834 g substance; 0.3273 g CO_2; 0.1205 g H_2O. 0.3827 g substance: 0.2142g AgBr. Found %: C 48.66; H 7.31; Br 23.93; $C_{13}H_{23}O_4Br$. Calculated %: C 48.30; H 7.12; Br 24.73.

a - Methyl-δ-pentenylmalonic ester

To a solution of alcoholate, obtained from 11.5 g (0.5 g-atom) of metallic sodium and 130 ml of absolute alcohol, 160 g(1 mole) of malonic ester was added [20], followed by 82 g (0.5 mole) of 5-bromhexene-1. The mixture was heated on a bath to boiling for 12 hours, then, after cooling, was diluted with water, acidified with sulfuric acid, the reaction products extracted with ether, the ether extracts washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue fractionated in vacuo. At first a few grams of the initial bromide (up to 70° at 4 mm) came over, then 71 g of malonic ester (71-73° at 4 mm) and finally 91 g of a-methyl-δ-pentenylmalonic ester of b.p. 110-111° at 2 mm. The resulting ester was in the form of a colorless oily liquid, almost odorless (yield 75.2% of theoretical):

d_4^{20} 0.9809; n_D^{20} 1.4397; MR_D 64.96; calculated 65.08.
0.1112 g substance; 0.2630 g CO_2; 0.0910 g H_2O. Found %: C 64.50; H 9.09. $C_{13}H_{22}O_4$.
Calculated %: C 64.46; H 9.09.

12 g of the substance was saponified while heating by a solution of 10 g KOH in 50 ml of 95% alcohol for 1.5 hours, the liquid diluted further with water, and the alcohol distilled off, the residue acidified by sulfuric acid and extracted 5 times with ether. The ether extraction was dried with anhydrous calcium chloride, and after vaporization of the ether, 8.8 g (95.6% of theory) of the dicarboxylic acid was deposited, which, after two recrystallizations from benzene, had a stable melting point of 106-107°.

0.2134 g substance: 0.4538 g CO_2; 0.1440 g H_2O. Found %: C 58.04; H 7.45. $C_9H_{14}O_4$.
Calculated %: C 58.06; H 7.53.

7.8 g of a-methyl-δ-pentenylmalonic acid was heated for 2 hours in a small flask with a reflux condenser, in a bath of Wood's metal to 180-200°. The liquid, 5-methylheptene-1-ic acid-6, remaining in the flask, boiled at 229-231° (709 mm) upon distilling from a Wurtz flask. The yield was 4.8 g, or 81.3% of theoretical; d_4^{20} 0.9358; n_D^{20} 1.4420; MR_D 40.14; calculated 40.21.

0.2572 g substance: 0.6354 g CO_2; 0.2296 g H_2O. Found %: C 67.38; H 9.92. $C_8H_{14}O_2$.
Calculated %: C 67.60; H 9.86.

Addition of HBr to a-methyl-δ-pentenylmalonic Ester. 30 g of a-methyl-δ-pentenylmalonic ester was dissolved in 50 ml of ether and gaseous hydrogen bromide was passed through the solutıon cooled in a mixture of snow and salt, to an increase in weight of 23 g. After standing overnight at room temperature, the liquid was poured into water, the reaction product separated, washed with dilute soda solution, then with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue distilled in vacuo. At the same time, about 10 g of initial unsaturated ester was recovered (b.p. 112-113° at 2.5 mm) and 20.8 g of fraction distilling at 143-144° (2.5 mm) and representing δ-brom-a-methylamylmalonic ester (a mixture of stereoisomers); d_4^{20} 1.2075; n_D^{20} 1.4616; MR_D 73.49; calculated 73.31.

0.2429 g substance; 0.4298 g CO_2; 0.1557 g H_2O. 0.2903 g substance; 0.1682 g AgBr. Found %: C 48.21; H 7.12; Br 24.67; $C_{13}H_{23}O_4Br$. Calculated %: C 48.30; H 7.12; Br 24.73.

The substance was in the form of a colorless, oily liquid with the odor of haloidalkylmalonic ester.

The yield (taking into account the initial substance recovered) was 78.1% of theory.

Cyclization of δ-brom-α-methylmalonic ester. 36 g (0.11 mole) of δ-brom-α-methylamylmalonic ester was added to an alcoholate solution prepared from 2.6 g (0.11 g-atom) of metallic sodium and 60 ml of absolute alcohol. Vigorous reaction took place, with strong evolution of heat from the mixture, and precipitation of sodium bromide. The mixture was further heated to boiling on a bath for 2 hours, and upon cooling was poured into acidified water, the reaction products extracted with ether, the ether extract washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue distilled in vacuo, which resulted in 23.4 g (87.2% of theory) of substance, boiling at 105-106° (4 mm) d_4^{20} 1.0159; n_D^{20} 1.4448; MR_D 63.35; calculated: 63.34.

0.2502 g substance: 0.5916 g CO_2; 0.2055 g H_2O. Found %: C 64.46; H 9.12. $C_{12}H_{22}O_4$.
Calculated %: C 64.49; H 9.12.

10.2 g of the resulting ester was saponified with a solution of 10 g KOH in 35 ml of 60% alcohol for 1 hour. After dilution with water, removal of the alcohol by distillation, and acidification of the solution with dilute acid, the saponification product separated in the form of a thick, viscous oil, partially crystallizable upon standing. The crystals were filtered with suction and after recrystallization from aqueous formic acid, melted at 81°, thus representing the same acid ester of cis-2,5-dimethylcyclopentane-1,1-dicarboxylic acid as was obtained in the experiment with 2,5-dibromhexane. A mixture of the substances also melted at 81°, by which was finally proven their identity.

The part of the saponification products which remained liquid was not examined further because of its small volume.

ε-Bromamylmalonic Ester

The pentamethylenebromide required for the given experiment was prepared according to the method of Braun [22] and possessed the following characteristics: b.p. 75-77° at 3 mm; d_4^{20} 1.6966; n_D^{20} 1.5140.

6.9 g (0.3 g atom) of metallic sodium was dissolved in 100 ml of absolute alcohol, and 192 g (1.2 mole) of malonic ester was then added, followed by 138 g (0.6 mole) of pentamethylene bromide. The mixture was heated on a bath with reflux condenser for four hours, and then was poured into water, the reaction products extracted with ether, the ether extract washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue fractionated in vacuo. Upon distillation there was obtained: 1) a mixture of malonic ester with pentamethylene bromide, b.p. up to 80° at 3 mm - 234 g; 2) a fraction with b.p. 151-154° at 3 mm - 56 g, and 3) the distillation residue weighing 17 g. The yield of 151-154° fraction was equal to 60.4% of theory.

In the second experiment an excess of pentamethylene bromide was not used. From 6.9 g of sodium, 192 g of malonic ester and 69 g of pentamethylene bromide, there was obtained, by the preceding method, 38 g of ε-bromamylmalonic ester (40.9% of theory).

Upon repeated distillation in vacuo, ε-bromamylmalonic ester boiled at 144-145° (1.5 mm) and was in the form of a colorless, viscous liquid with the characteristic odor of bromalkylmalonic ester; d_4^{20} 1.2310; n_D^{20} 1.4603; MR_D 68.86; calculated 68.69.

0.2144 g substance; 0.3657 g CO_2; 0.1316 g H_2O. 0.2583 g substance: 0.1576 g AgBr. Found %: C 46.52; H 6.82; Br 26.03. $C_{12}H_{21}O_4Br$. Calculated %: C 46.60; H 6.80; Br 25.88.

From the residues combined from the first distillations, there was obtained when they were distilled in vacuo, a fraction with b.p. 190° at 1 mm, which represents the ester of heptane-1,1,7,7-tetracarboxylic acid; d_4^{20} 1.0710; n_D^{20} 1.4460; MR_D 96.60; calculated 96.46.

0.1836 g substance: 0.3950 g CO_2; 0.1372 g H_2O. Found %: C 58.67; H 8.30. $C_{19}H_{32}O_8$.
Calculated %: C 58.76; H 8.25.

The substance was saponified with an alcoholic solution of caustic alkali; the heptane-1,1,7,7-tetracarboxylic acid formed at the same time was heated in Wood's metal to 200°. The resulting azeloic acid melted at 106-107° after recrystallization from benzene [23].

Cyclization of ε-Bromamylmalonic Ester. To a solution of 3 g (1.13 g-atom) of sodium in 70 ml of absolute alcohol, 40 g (0.13 mole) of ε-bromamylmalonic ester was added. At that time strong heat evolution resulted, and the liquid started to boil. The mixture was further heated on a bath for 2 hours, and after cooling, water was added, the separated oil extracted with ether, the ether extract washed with water, dried with anhydrous calcium chloride, ether distilled off, and the residue distilled in vacuo, from which there resulted a

fraction with b.p. 100-103° at 2 mm in the amount of 17.8 g (60.1%). The residue from distillation weighed 8.5 g.

The 100-103° fraction, upon repeated distillation, boiled at 100° (2 mm) and represented the ester of cyclohexane-1,1-dicarboxylic acid; d_4^{20} 1.0405; n_D^{20} 1.4482; MR_D 58.68; calculated 58.72.

ε-Iodamylmalonic Ester

To a solution of 45 g sodium iodide in 120 ml of acetone, 40.2 g of ε-bromamylmalonic ester was added. The solution was heated to boiling on a bath for 2 hours, during which a greater part of the acetone boiled off, water was added to the residue to dissolve the sodium bromide which had precipitated during the reaction, the reaction product was extracted with ether, the ether extract; washed with a weak solution of hyposulfite, then with water, was then dried with anhydrous calcium chloride, the ether distilled off, and the residue distilled in vacuo. 41.2 g of liquid of light yellow color, with b.p. 162° at 3 mm, was obtained upon distillation. The yield was 89.5% of theoretical; d_4^{20} 1.3808; n_D^{20} 1.4844; MR_D 73.81; calculated 73.72.

0.1686 g substance; 0.2490 g CO_2; 0.0912 g H_2O. 0.2178 g substance: 0.1427 g AgI. Found %: C 40.27; H 6.01; I 35.41. $C_{12}H_{21}O_4I$. Calculated %: C 40.45; H 5.90; I 35.67.

Cyclization of ε-iodamylmalonic ester. 40 g (0.11 mole) of ε-iodamyl malonic ester was added to the alcoholate solution from 2.7 g (0.11 g-atom) of metallic sodium and 50 ml of absolute alcohol. After completion of quite a vigorous reaction, accompanied by strong heat evolution and separation of sodium iodide, the mixture was heated on a bath to boiling for 2 hours. After cooling, water was then added, the separated oil extracted with ether, the ether extract washed with weak hyposulfite solution, then with water, dried with anhydrous calcium chloride, the ether distilled off, the ether residue distilled in vacuo, at which time 15.7 g of cyclohexane-1,1-dicarboxylic ester, with b.p. 110° at 4 mm, passed over into the receiver. There remained in the flask 7 g of viscous, non-distillable oil. The yield was equal to 61.6% of theoretical.

γ-Iodpropylmalonic Ester

160 g (1 mole) of malonic ester was added to an alcoholate solution prepared from 5.75 g (0.25 g-atom) of metallic sodium and 75 ml of absolute alcohol, and then 148 g (0.5 mole) of trimethylene iodide, obtained by reaction of sodium iodide in acetone solution with trimethylene bromide, and having a b.p. of 83-85° at 1.5 mm. The reaction mixture was heated on a bath to boiling for 4 hours, was then cooled, poured into water, the separated oil isolated, the water layer extracted with ether, the ether extract combined with the main bulk of reaction product, washed with a weak solution of hyposulfite, then with water, dried with anhydrous calcium chloride, and after removal of the ether by distillation, fractionated in vacuo.

At first the mixture of malonic ester with trimethylene iodide (the fraction with b.p. up to 135° at 2 mm), was distilled, at which there passed over γ-iodpropylmalonic ester with b.p. 135-146° at 2 mm in the amount of 47.6 g (58%). Upon repeated distillation, the product boiled chiefly at 138° (1.5 mm); d_4^{20} 1.4601; n_D^{20} 1.4869; MR_D 64.60; calculated 64.49.

In the second experiment, without the use of trimethylene iodide excess, 34 g (41.4%) of γ-iodpropylmalonic ester was obtained from 5.75 g (0.25 g-atom) of sodium, 160 g (1 mole) of malonic ester and 74 g (0.25 mole) of trimethylene iodide.

Cyclization of γ-iodpropyl ester. 49.2 g (0.15 g-atom) of γ-iodpropylmalonic ester was added to a solution of 3.5 g (0.15 g-atom) of metallic sodium in 80 ml of absolute alcohol. After completion of the spontaneous heat evolution, the mixture was heated on a bath to boiling for 2 hours. The flask contents were then poured into water acidified with sulfuric acid, the reaction product extracted with ether, the ether extract washed with a weak solution of hyposulfite, then with water, dried with anhydrous calcium chloride, and the ether distilled off. The residue, upon distillation in vacuo, boiled at 91° (5 mm). The yield was 21 g of cyclobutane-1,1-dicarboxylic ester, which comprised 70% of theory; d_4^{20} 1.0475; n_D^{20} 1.4360; MR_D 49.92; calculated 49.95.

Cyclization of γ-brompropylmalonic ester. To the alcoholate solution obtained from 6.9 g (0.3 g-atom) of metallic sodium and 160 ml of absolute alcohol, 85 g (0.3 mole) of γ-brompropylmalonic ester [9] was added. The mixture was heated on a bath to boiling for 4 hours, after which it was cooled and poured into water acidified with sulfuric acid. The separated oil was extracted with ether, the ether extraction washed with water, dried with anhydrous calcium chloride, the ether distilled off, and the residue distilled in vacuo. There was obtained 43 g (71.7 %) of cyclobutane-1,1-dicarboxylic ester, boiling at 103° (10 mm); d_4^{20} 1.0472; n_D^{20} 1.4363; MR_D 49.97; calculated 49.95.

β-Chlorethylmalonic Ester

160 g (1 mole) of malonic ester was first added to an alcoholate solution from 5.75 g (0.25 g-atom) of metallic sodium and 75 ml of absolute alcohol, followed by 99 g (1 mole) of ethylene chloride. The mixture was heated on a water bath to boiling for 4 hours, subsequently cooled, poured into water, the lower layer separated, and the upper layer extracted twice with ethylene chloride. The solutions were combined, washed with water, dried with anhydrous calcium chloride, and the ethylene chloride then distilled off at ordinary pressure with a fractionating column. The residue was redistilled in vacuo, and 147 g of a mixture of malonic ester and cyclopropane-1,1-dicarboxylic ester (the fraction with b.p. 80° at 3 mm) and 4.5 g of substance boiling at 121-124° (3 mm) were obtained. The yield constituted 8% of theoretical, on the basis of β-chlorethylmalonic ester.

Fractions combined from the two experiments, with b.p. 121-124°, boiled mainly at 122-123° (3 mm) after repeated distillation; d_4^{17} 1.1300; n_D^{17} 1.4425; MR_D 52.14 [1]; calculated 51.94.

The fraction with b.p. up to 80° was separated, according to the method of Kuster and Grassner [2], into cyclopropane-1,1-dicarboxylic ester with a yield of 64.52% of theory, by saturation of the fraction with gaseous hydrogen bromide, fractional distillation of the mixture of malonic and β-brom-ethyl-malonic esters formed, and reconversion of the latter into cyclopropane-1,1-dicarboxylic acid with the help of sodium alcoholate.

SUMMARY

1. Haloid-substituted alkylmalonic esters are formed in good yields by reaction of sodium malonic ester with 1,3-, 1,5-, and 1,6-dihaloid derivatives under conditions which inhibit the side reactions, the value of which is determined by the excess of dihaloid-derivative used for the reaction, and can be calculated beforehand.

2. When sodium malonic ester and 1,2-and 1,4-dihaloid derivatives are reacted under the same conditions, β- and δ-haloidalkylmalonic esters are obtained in very poor yield, because the reaction proceeds further with the formation of cyclic polymethylene.

3. δ-Brom-α-methylamylmalonic ester is obtained by addition of HBr to α-methyl-δ-pentenylmalonic ester.

4. Upon reaction of sodium alcoholate with haloidalkylmalonic esters, a five-membered ring is formed with the greatest of ease in about 90% yield of theoretical, four-membered with a yield of about 70%, three-membered - 65%, six-membered, about 60% and seven-membered - 3%.

5. The nature of the halogen in the haloidalkylmalonic ester affects very little the yield of the cyclic ester.

LITERATURE CITED

[1] N. Ya. Demyanov and V. V. Feofilaktov, J. Gen. Chem. 9, 349 (1939). [2] W. Kuster, F. Grassner, Z. physiol. chem.145, 45 (1925). [3] V.P. Golmov, B. A. Kazansky, Proc. Acad. Sci., U.S.S.R., 33, 37 (1941). [4] R. Willstatter, Frtlinger, Ann., 326, 99 (1903). [5] F. H. Case, J. Am. Chem. Soc., 55, 2927 (1933). [6] B.A. Kazansky, M. Yu. Lukina, Bull. Acad. Sci, U.S.S.R., Div. Chem. Sci, 47 (1951). [7] V.P. Golmov, J. Gen. Chem. 22, 109 (1952).* [8] K. Ziegler, K. Weber, Ann., 512, 164 (1934). [9] V.P. Golmov, J. Gen. Chem. 19, 1679 (1949)**. [10] H. M. Walborsky, J. Am. Chem. Soc., 71, 2941 (1949). [11] C.N. Riiber, Ber., 44, 2974 (1911). [12] Wislicenus, Ber,, 34, 2565 (1901). [13] T.L. Jacobs, W. H. Florsheim, J. Am. Chem. Soc., 72, 256 (1950). [14] Dox, Joder, J. Am. Chem. Soc., 43, 2098 (1921). [15] Roger, Adams, Organic Synthesis, 8 (1921)j. [16] A. J. Vogel, J. Chem. Soc., 1488 (1929). [17] Wibaut, Rec. trav. chim. 58, 335 (1939). [18] C. S. Marvel, A. L Tanenbaum, J. Am. Chem. Soc., 44, 2645 (1922). [19] E. Fischer, H. Blumenthal, Ber., 40, 107 (1907). [20] H. Leuchs, Ber., 44, 1507 (1911). [21] Prins, Rec. trav. chim., 42, 1050 (1923). [22] Synthesis of Organic Preparations 1, 124 (1949). [23] I. Heilbron and G. Benberry, A Dictionary of Organic Compounds, 1, 199 (1949). [24] H. Freundlich, G. Solomon, Ber., 66, 355 (1933). [25] G. M. Bennett, F. Heathcoat, A. N. Mosses, J. Chem. Soc., 1929, 2567. [26] D. C. Sayles, E.F. Degering, J. Am. Chem. Soc., 71, 3161 (1949). [27] M. S. Kharasch, P.S. Skell, P. Fischer, J. Am. Chem. Soc. 70, 1055, (1948).

* See Consultants Bureau, translation, p. 127

** See Consultants Bureau, translation, p. a-109

SELECTIVE MALONIC SYNTHESIS

## II. REACTION OF SODIUM MALONIC ESTER WITH 4-BROM-3-BROMETHYL-2-METHYLBUTANE

.V. P. Golmov and N. M. Afanasev

In the preceding articles by one of us [1,2], it was demonstrated that γ-haloidalkylmalonic ester inter-mediate product is obtained in good yield, up to 70% of theoretical, by reaction of sodium malonic ester with the bromide or iodide of trimethylene under the conditions favorable for good product yield. Upon reaction of sodium alcoholate with γ-haloidalkylmalonic ester, it transforms into a four-membered cyclic compound, with a yield also equal to approximately 70%. As a continuing study of the reaction of sodium malonic ester with dihaloidoderivatives, the authors in the present work have carried out an analogous reaction with 4-brom-3-bromethyl-2-methylbutane, for the purpose of determining whether or not the isopropyl group contained in the molecule of initial dibromide exerts any influence on the yield of γ-bromalkylmalonic ester, and also upon the rate of cyclization of the latter. The method selected by the authors for synthesis of the latter consisted of reacting monochlormethyl ester with the sodium derivative of isopropylmalonic ester, of transformation of the methoxymethylisopropylmalonic ester formed thereby into β-methoxy-a-isopropylpropionic acid, and of reduction of the ester of the latter (acid) into β-methoxy-a-isopropylpropyl alcohol with resulting interaction of it with a mixture of hydrogen bromide and sulfuric acid:
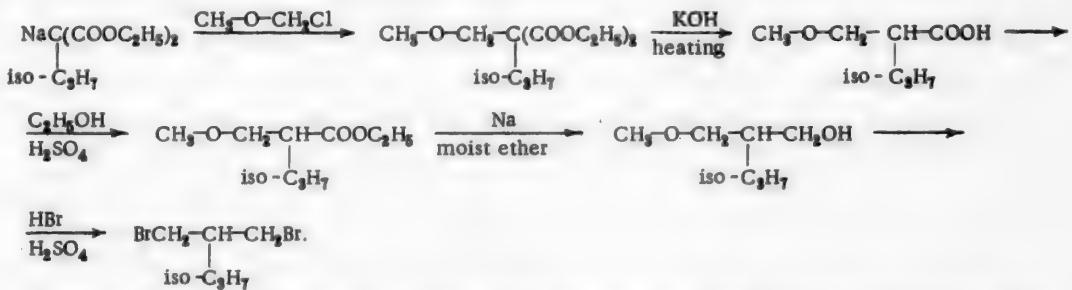
Execution of the above-mentioned reactions clarified the fact that the liquid β-methoxy-a-isopropyl-propionic acid, ("β-methoxymethyl isovaleric") acid, obtained earlier by Simonsen [3] by the same method, in reality is a mixture of crystalline β-methoxy-a-isopropylpropionic acid (m.p. 37-38°) with unsaturated liquid a-isopropylacrylic acid, obtained earlier by Semenov via another method [4].

Upon reaction of sodium malonic ester with 4-brom-3-bromethyl-2-methylbutane, γ-brom-β-isopropyl-propylmalonic ester is obtained in only 18% yield, because in the case given, even under conditions which are not favorable to cyclization, the reaction proceeds further to the formation of 1-isopropylcyclobutane-3,3-di-carboxylic ester:
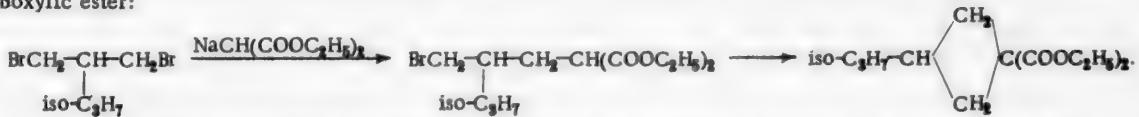
Under the same conditions, γ-iodopropylmalonic ester, for example, is obtained in a yield of 58%, and the cyclobutane-1,1-dicarboxylic ester in negligible quantity [2]. Thus the isopropyl group, contained in the molecule of original bromide, exerts a significant influence on the course of selective malonic synthesis.

Upon reaction of sodium alcoholate with the isolated γ-brom-β-isopropylpropylmalonic ester, the latter transforms into 1-isopropylcyclobutane-3,3-dicarboxylic ester, with a yield 70% of theory, which is exactly the same as γ-brom- or γ-iodpropylmalonic ester, into cyclobutane-1,1-dicarboxylic ester.

This points to the conclusion that the isopropyl group does not affect the velocity constant for four-membered ring formation, and thus explains the unusual course for the first phase of the reaction; it must be admitted that the reversible reaction between sodium malonic ester and γ-brom-β-isopropylpropylmalonic ester is shifted to the right.

$$\underset{\text{iso-}C_3H_7}{BrCH_2-CH-CH_2CH(COOC_2H_5)_2} + NaCH(COOC_2H_5)_2 \rightleftharpoons \underset{\text{iso-}C_3H_7}{BrCH_2-CH-CH_2-CNa(COOC_2H_5)_2} + CH_2(COOC_2H_5)_2.$$

As the result, the sodium derivative of γ-brom-β-isopropylpropylmalonic ester should be formed in the reaction mixture, during the process of reaction, in increased concentration, and its cyclization should proceed more rapidly than with other γ-haloidalkylmalonic esters with a non-branched carbon chain.

EXPERIMENTAL

As initial substances for the present work served: isopropylmalonic ester, with a b.p. of 77-79° at 3 mm [5], obtained by reaction of sodium malonic ester with isopropyl iodide, and monochlormethyl ester, with a b.p. of 55-60° [6]. In view of the fact that the authors in many cases have departed from the directions contained in the work of Simonsen [3], the experimental methods are cited in full.

Methoxymethylisopropylmalonic Ester. 11.5 g (0.5 mole) of powdered metallic sodium was introduced into 300 ml of dry ether, and thereto was added 101 g (0.5 mole) of isopropylmalonic ester. During approximately one hour all of the sodium went into solution. 50 g (0.62 mole) of chlormethyl ether was then added from a dropping funnel, with water cooling, at such a speed as to avoid boiling of the ether. After 24 hours, the reaction mixture was poured into water, the ether layer separated, and the water layer extracted twice with ether. The combined ether extracts were dried by anhydrous calcium chloride, and the ether distilled off. The combined residues from six experiments gave back, upon vacuum distillation, 130 g of isopropylmalonic ester (the fraction with a b.p. of 77-80° at 3 mm) and 431 g of methoxymethylisopropylmalonic ester, boiling at 100-101° (3 mm). The yield amounted to 75.3% of theory, calculated on the basis of isopropylmalonic ester entered into reaction; d_4^{20} 1.0223; n_D^{20} 1.4320; MR_D 62.41; calculated 62.54.

0.3047 g substance: 0.6534 g CO_2; 0.2422 g H_2O. Found %: C 58.48; H 8.83. $C_{12}H_{22}O_5$. Calculated %: C 58.53; H 8.94.

Saponification of Methoxymethylisopropylmalonic Ester. 562 g of methoxymethylisopropyl malonic ester was gradually added to a heated solution of 347 g of KOH in 1200 ml of 33% alcohol. The mixture was boiled on a bath for 2 hours, the alcohol was distilled off completely, and to the cooled residue was added a small excess of dilute sulfuric acid, and the liquid extracted several times with ether. The combined ether extracts were dried with anhydrous calcium chloride, and the ether distilled off, and the residue refluxed on an oil bath at 180°, until carbon dioxide evolution ceased. The decarboxylated liquid acid remaining was fractionally distilled in vacuo, during which time 97 g of fraction was obtained, b.p. 69-72° at 4 mm, and 201 g of fraction with b.p. 103-105° at 4 mm. The latter, upon standing, crystallized completely.

a-Isopropylacrylic Acid. The 69-72° (at 4 mm) fraction upon repeated distillation boiled in the range 185-186° (708 mm) and, judging from the constants and results of elementary analysis, represented a-isopropyl-acrylic acid. Yield 37.2% of theoretical; d_4^{20} 0.9579; n_D^{20} 1.4336; MR_D 31.00; calculated 30.98.

0.3030 g substance: 0.7025 g CO_2; 0.2450 g H_2O. Found %: C 63.23; H 8.98. $C_6H_{10}O_2$. Calculated %: C 63.16; H 8.77.

The acid was converted into the chloranhydride by reaction with phosphorous pentachloride, the former of which was introduced, dropwise and with cooling, into concentrated ammonia solution. The amide, thus obtained, melted at 104-105° after recrystallization from chloroform.

0.2539 g substance: 22.1 ml 0.1 N H_2SO_4 Kjeldahl. Found %: N 12.19. $C_6H_{11}ON$. Calculated %: N 12.39.

The ethyl ester of a-isopropylacrylic acid was obtained by heating on a water bath for 4 hours with triple the volume of absolute alcohol, to which was added 10% by volume of concentrated sulfuric acid. With heating terminated, the mixture was poured into water, extracted with ether, ether extraction washed with water, dried with $CaCl_2$, the ester distilled off, and the residue redistilled at 149-152° (710 mm). Yield 78.8% of theoretical; d_4^{20} 0.8950; n_D^{20} 1.4210; MR_D 40.23; calculated 40.33.

0.1996 g substance: 0.4941 g CO_2; 0.1783 g H_2O. Found %: C 67.52; H 9.93. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.86.

As evidence for unsaturation, bromine was added to the acid. 6.3 g (0.055 mole) of the acid was dissolved in 30 ml of dry ether, and to the solution was added, dropwise, with water cooling, 10 g (0.062 mole) of bromine. After 4 hours, the reaction mixture was poured into water, agitated with a solution of Na_2CO_3 to the point of discoloration, the ether layer separated, dried with $CaCl_2$, and the ether distilled off. The residue crystallized almost completely upon standing. The crystals were sucked off, and after recrystallization from chloroform, melted at 88-89°. Yield 14 g, or 62.7% of the theoretical.

0.3150 g substance: 0.4325 g AgBr. Found %: Br 58.76. $C_8H_{10}O_2Br_2$. Calculated %: Br 58.39.

For addition of bromine to the ethyl ester of a-isopropylacrylic acid, 10 g of the latter was dissolved in 40 ml of dry ether, and to the solution was added dropwise, and with cooling, 12 g of bromine. After treatment, according to the preceding, an oil was obtained with a b.p. of 98-100° at 4 mm, representing the ethyl ester of a,β-dibrom-a-isopropylpropionic acid; d_4^{20} 1.5751; n_D^{20} 1.5751; n_D^{10} 1.4975; MR_D 56.14; calculated 56.33.

0.3415 g substance: 0.4231 g AgBr. Found%: Br 53.00. $C_8H_{14}O_2Br_2$. Calculated %: Br 52.98.

<u>β-Methoxy-a-isopropylpropionic Acid</u>. The 103-105° (4 mm) fraction, obtained as the result of saponification of methoxymethylisopropylmalonic ester, was found to be β-methoxy-a-isopropylpropionic acid (yield 60.5%). After recrystallization from ether, it appeared as large, colorless crystals, melting at 37-38°; d_4^{40} 0.9911; n_D^{40} 1.4242; MR_D 37.60; calculated 37.70.

0.1964 g substance: 0.4132 g CO_2; 0 1673 g H_2O. Found %: C 57.38; H 9.46. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.58.

8 g of the acid was added to 12 g of PCl_5, and the liquid mixture formed was fractionated. The chloranhydride of β-methoxy-a-isopropylpropionic acid (b.p. 148-151°; d_4^{20} 1.0226; n_D^{20} 1.4307; MR_D 41.62; calculated 41.42) was dissolved in ether, which was saturated with ammonia and in addition the solution was saturated with NH_3; the ether solution was steamed off to dryness, and the residue extracted with chloroform; the amide obtained from the chloroform solution melted at 113° after recrystallization from water.

0.1101 g substance: 7.4 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 9.41. $C_7H_{15}O_2N$. Calculated %: N 9.65.

For esterification, 226 g of β-methoxy-a-isopropylpropionic acid was added to a solution of 62 ml of H_2SO_4 (specific gravity 1.84) in 620 ml of absolute alcohol. The mixture was boiled on a water bath for 4 hours, then was poured into 2 liters of water, the ester separated, the water layer extracted with ether, the ether extract combined with the main product, washed with water, dried with $CaCl_2$, the ether distilled off, and the residue redistilled in vacuo, at which time it boiled at 35 mm in the 95-97° range, yield 236 g, or 90% of the theoretical; d_4^{20} 0.9332; n_D^{20} 1.4180; MR_D 46.98; calculated 47.06.

0.1846 g substance: 0.4196 g CO_2; 0.1744 g H_2O. Found %: C 61.69; H 10.49. $C_9H_{18}O_3$. Calculated %: C 62.07; H 10.35.

Upon saponification of the β-methoxy-a-isopropylpropionic acid ester, there is obtained a mixture of β-methoxy-a-isopropylpropionic acid and a-isopropylacrylic acid of approximately the same composition as upon saponification of methoxymethylisopropylmalonic ester.

<u>β-Methoxy-a-isopropylpropyl Alcohol</u>. The authors applied the method of Prins [7] for reduction of the ethyl ester of β-methoxy-a-isopropylpropionic acid. Into a flask equipped with dropping funnel, mechanical stirrer, and thermometer reaching almost to the bottom of the flask, cooled by a salt-ice mixture, 150 ml of a saturated solution of sodium acetate and 70 g (0.4 mole) of β-methoxy-a-isopropylpropionic acid ethyl ester, dissolved in 210 ml of diethyl ether, was added. 56 g (2.4 g-atoms) of metallic sodium was gradually added, with slow mixing, to the mixture at a temperature of −8 to −3°, and 30% acetic acid dropwise, simultaneously. Total addition took about 10 hours. Water was then added to dissolve the precipitated salt, the ether was separated, and the water layer twice extracted with ether. The combined ether solutions were dried with anhydrous potash, the ether distilled off, and the residue fractionated in vacuo, and the fraction collected boiled at 92-94° (38 mm). A considerable quantity of brownish viscous mass remained in the flask. To purify from the admixture of initial ester, the alcohol obtained was boiled with caustic potash solution, then salted out with potash, the separated layer set aside, the water layer extracted with ether, the ether extract dried with anhydrous potash,

and the ether distilled off. Upon distillation in vacuo, the residue boiled at 91-93° (26 mm), and represented pure β-methoxy-α-isopropylpropyl alcohol, in the form of an oily liquid, turning yellow rapidly in the air, possessing a characteristic camphor odor, and quite soluble in water. From 236 g of initial ester, 90 g of β-methoxy-α-isopropylpropyl alcohol was obtained, i.e., 50.5% of the theoretical yield; d_4^{20} 0.9112; n_D^{20} 1.4322; MR_D 37.59; calculated 37.69.

0.2271 g substance: 0.5302 g CO_2; 0.2472 g H_2O. Found %: C 63.67; H 12.10. $C_7H_{16}O_2$. Calculated %: C 63.64; H 12.14.

The p-nitrobenzoate of β-methoxy-α-isopropylpropyl alcohol, obtained by the usual procedure of reaction of p-nitrobenzoyl chloride with alcohol in pyridine, melted at 236-237° after recrystallization from alcohol.

4-Brom-3-brommethyl-2-methylbutane. 76 g of β-methoxy-α-isopropylpropyl alcohol was mixed with 380 g of hydrobromic acid (d. 1.54), and to the mixture was next added 120 ml of sulfuric acid (d. 1.84), and the liquid boiled for 6 hours on an oil bath. During the same period, the mixture became intensely dark. After cooling, the liquid was poured into water, carefully agitated (vigorous agitation causes formation of a very stable emulsion), the lower bromide layer separated, and the upper extracted 4 times with ether. The ether extracts, combined with the main bulk product, were washed with soda solutions, then with water, dried with $CaCl_2$, the ether distilled off, and the residue redistilled in vacuo. Upon distillation, we obtained 82 g of heavy oily liquid, becoming brownish upon exposure to air, and having a b.p. of 82-84° at 9 mm. For purification, the bromide obtained was shaken twice with half the volume of concentrated sulfuric acid, then washed with water, dried with $CaCl_2$, and redistilled in vacuo. Purified in this manner, the 4-brom-3-brommethyl-2-methylbutane was in the form of a colorless heavy liquid of characteristic odor, with a b.p. of 90° at 13 mm. Yield 58.9% of theoretical; d_4^{20} 1.6132; n_D^{20} 1.5076; MR_D 45.44; calculated 45.07.

0.3977 g substance: 0.4328 g CO_2; 0.1840 g H_2O. 0.3091 g substance: 0.4762 g AgBr. Found %: C 29.68; H 5.14; Br 65.61. $C_6H_{12}Br_2$. Calculated %: C 29.51; H 4.92; Br 65.57.

Reaction of Sodium Malonic Ester with 4-Brom-3-brommethyl-2-methylbutane. 109 g (0.68 mole, 4 times the theoretical) of malonic ester was added to an alcoholate solution, prepared from 3.95 g (0.17 g-atom) of metallic sodium and 50 ml of absolute alcohol, followed by 85 g (0.34 mole) of 4-brom-3-brommethyl-2-methylbutane. The mixture was heated to boiling on a bath for 4 hours, after which the reaction became neutral. After cooling, the reaction mixture was poured into 400 ml of water, the reaction products separated, and the water layer extracted twice with ether. The ether extracts combined with the principal mass of product, were washed with water, dried with anhydrous calcium chloride, and the ether distilled off afterwards, and the residue fractionated in vacuo at 6 mm. From this there was obtained 138 g of fraction with b.p. 76-78° (a mixture of malonic ester with the initial dibromide), 9.5 g with b.p. 115-117° (1-isopropylcyclobutane-3,3-dicarboxylic ester —yield 46.1% of theoretical), 10 g with b.p. 154-158° (γ-brom-β-isopropylpropylmalonic ester, yield 18.2% of theoretical) and 10 g of residue, probably representing the ethyl ester of 3-isopropylpentane-1,1,5,5-tetracarboxylic acid.

1-Isopropylcyclobutane-3,3-dicarboxylic ester was a colorless liquid, almost without odor; d_4^{20} 0.9966; n_D^{20} 1.4374; MR_D 63.67; calculated 63.80.

0.1771 g substance: 0.4177 g CO_2; 0.1434 g H_2O. Found %: C 64.32; H 9.00. $C_{13}H_{22}O_4$. Calculated %: C 64.46; H 9.09.

The 154-158° fraction, upon repeated distillation in vacuo, boiled at 155-156°, and was in the form of a slightly yellowish liquid with an odor of haloidalkylmalonic ester; d_4^{20} 1.2088; n_D^{20} 1.4623; MR_D 73.50; calculated 73.31.

The substance gave a positive Beilstein test for halogen.

0.2571 g substance: 0.4584 g CO_2; 0.1676 g H_2O. 0.3914 g substance: 0.2179 g AgBr. Found %: C 48.62; H 7.24; Br 23.70. $C_{13}H_{23}O_4Br$. Calculated %: C 48.30; H 7.12; Br 24.73.

Cyclization of γ-Brom-β-isopropylpropylmalonic Ester. 1 g (0.04 g-atom) of metallic sodium was dissolved in 49 ml of absolute alcohol, and 13 g (0.04 mole) of γ-brom-β-isopropylpropyl malonic ester was added to the alcoholate solution after its cooling. The mixture was boiled on a bath for several hours, until the sodium derivative of the initial bromester, precipitated in the beginning, was dissolved. Subsequently, the reaction mixture was cooled, poured into water, the reaction product extracted with ether, washed with water, dried with $CaCl_2$, and the ether

distilled off. Upon distilling in vacuo, 5.9 g of 1-isopropylcyclobutane-3,3-dicarboxylic ester was obtained, with a b.p. of 118-120° at 7 mm, and 1.9 g of initial bromester was recovered. The yield of cyclic product was 70.2% of the theoretical, based upon γ-brom-isopropylpropylmalonic ester used. The residue in the flask weighed 1 g.

1-Isopropylcyclobutane-3,3-dicarboxylic Acid. To a warm solution of 42 g of caustic potash in 150 ml of 95% alcohol, was added 58 g of 1-isopropylcyclobutane-3,3-dicarboxylic ester. At the same time a large amount of precipitate separated out, which was dissolved upon addition of 25 ml water. After 2 hours heating on a bath at the boiling point of the liquid, 125 ml of water was added, and the alcohol distilled off completely. The cooled residue was acidified with dilute (1:1) sulfuric acid and extracted 7 times with ether. The ether extract was dried with calcium chloride, and after distilling off the ether, 41.5 g (93.1%) of crystalline acid was left, which, after being recrystallized three times from benzene, was obtained in the form of colorless flakes, melting at 168°.

0.1758 g substance: 0.3726 g CO_2; 0.1207 g H_2O. Found %: C 57.81; H 7.63. $C_9H_{14}O_4$. Calculated %: C 58.06; H 7.53.

The Diamide of 1-Isopropylcyclobutane-3,3-dicarboxylic Acid was obtained, according to the method of Demyanov and Telnov [8] by reaction of a concentrated solution of ammonia with 1-isopropylcyclobutane-3,3-dicarboxylic ester at normal temperature for one month. After recrystallization from water, the obtained amide melted with decomposition at 211°.

0.2522 g substance: 27.0 ml 0.1 N H_2SO_4 (Kjeldahl.) Found %: N 14.99. $C_9H_{16}O_2N_2$. Calculated %: N 15.21.

SUMMARY

1. When sodium malonic ester is reacted with 4-brom-3-brommethyl-2-methylbutane, contrary to γ-brompropyl- and γ-iodopropylmalonic ester, there is formed the γ-brom-β-isopropylpropylmalonic ester with a yield of only 18% of the theoretical, because in this instance the reaction goes further, with the formation of 1-isopropylcyclobutane-3,3-dicarboxylic ester as the principal product.

2. A branched chain in the γ-brom-β-isopropylpropylmalonic ester molecule does not affect the rate of cyclization of the latter; upon its reaction with sodium alcoholate, it transforms into a four-membered cyclic compound with a yield 70% of theory, i.e., approximately the same as the other γ-haloidalkylmalonic esters, that have been studied up to the present time.

LITERATURE CITED

[1] V. P. Golmov, J. Gen. Chem. 19, 1679 (1949).*

[2] V. P. Golmov, J. Gen. Chem. 22, 1948 (1952). **

[3] Simonsen, J. Chem. Soc. 93, 1777 (1908).

[4] Semenov, Journal of the Russian Chemical Society 31, 115 (1899).

[5] Conrad, Bischoff, Ann. 204, 144 (1880).

[6] Syntheses of Organic Compounds 1, 278 (1949).

[7] Prins, Rec. trav. chim. 42, 1050 (1923).

[8] Demyanov and Telnov, Bull. Acad. Sci. USSR 1937, 533.

---

* See Consultants Bureau English translation page 1993 ff.

** See Consultants Bureau English translation page a-109.

ISOMERISM OF ALLENE HYDROCARBONS UNDER THE INFLUENCE OF SILICATES

IX. ISOMERISM OF HEXADIENE-1,2

Ya. M. Slobodin

In 1885, A. E. Favorsky [1] proposed a mechanism for the isomeric transformation phenomenon of the hydrocarbon series C_nH_{2n-2}, from which resulted the rule that monosubstituted acetylenes transform into disubstituted acetylenes via the corresponding allene forms. These schemes did not foresee the transformation of cumulative dienes into conjugated dienes. Later, A. E. Favorsky considered these reactions to be intra-molecular regroupings, where alcoholic alkali functions in the role of catalyst [2].

The isomerism of allene hydrocarbons is thought to take three courses: 1) transformation into mono-substituted acetylenes, 2) transformation into disubstituted acetylenes and 3) transformation into conjugated dienes.

Transformation of allenes into monosubstituted acetylenes occurs easily upon heating with metallic sodium. In this case the process is not reversible, due to the fact that the monosubstituted acetylene formed is derived from the reaction sphere in the form of its sodium derivative [1-3]. The authors, applying floridin as the catalyst, have proved the reversibility of these transformations in the case of allene and allylene [4], methylallene and ethylacetylene [5], asymmetrical dimethylallene and isopropylacetylene [6], and others. The data obtained by us for equilibrium in the allene-allylene system were found to be of the same order as the theoretical calculations, based upon spectroscopic data [7]. Still earlier, Kucherov [8] and Favorsky and Debu [9] observed the transformation of asymmetrical dimethylallene into isopropylacetylene.

The transformation of allenes into disubstituted acetylenes, as well as formation of the latter from monosubstituted acetylenes, has been observed frequently. This draws attention to the fact that in a majority of cases, upon transformation of monosubstituted acetylenes into disubstituted acetylenes, it is not possible to detect the corresponding allenes, which are thought to be intermediate forms, although their stability is sufficient for at least partial existence under the conditions of the reaction [14-17].

On the other hand, in a majority of the cases, when the principal products of transformation of the monosubstituted acetylenes are found to be allenes, it is not possible, as a rule, to find disubstituted acetylenes in the reaction mixture [18]. In addition, when allenes are transformed into disubstituted acetylenes, it is always possible to detect among the reaction products smaller or larger quantities of the monosubstituted acetylenes.

A review of the literature data indicates that the allenes are more regularly transformed into conjugated dienes [10-13]. This also follows from energy considerations [19-20].

On the basis of investigations of transformations of hydrocarbons of the series C_nH_{2n-2} in the presence of silicate, we [21-22] have expressed an assumption that the process of isomerism for monosubstituted acetylenes should be divided into two independent processes. The first one consists in transformation of mono-substituted acetylenes into conjugated dienes, through the intermediate allene forms. The second process, independent of the first, consists of transformation of monosubstituted acetylenes directly into disubstituted acetylenes:
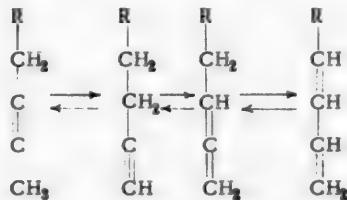
Proof of the reversibility of transformations of the separate systems of this general scheme has been obtained on a sufficient variety of compounds.

In the present investigation, the transformation of hexadiene-1,2 in the presence of floridin and of chromic oxide has been studied. In the combined dispersion spectrum of the initial hydrocarbon intense lines are observed with frequencies of 1039, 1096 and 1129 centimeter^{-1}, which characterize the allene grouping. Lines in the frequency interval 1600-1700 centimeter^{-1}, which characterize double bonds, are completely absent. A very faint line was detected with a frequency of 2234 centimeter^{-1}, indicating the presence of small amounts (less than 10%) of disubstituted acetylene in the hydrocarbon.

In the combined dispersion spectrum of allene isomerized in the presence of floridin, frequencies of 1039, 1096 and 1129 centimeter^{-1} were weakened. Lines with frequencies 1655 and 1668 centimeters^{-1}, characterizing double bonds, appeared. Moreover, there appeared lines with frequencies of 2123, 2237 and 2303 centimeter^{-1}. The frequency, 2123 centimeter^{-1}, points to the presence of monosubstituted acetylene in the hydrocarbon mixture after isomerization in the presence of floridin. The frequencies, 2237 and 2303 centimeter^{-1} indicate disubstituted acetylene in the isomerized hydrocarbon. Moreover, the frequency of 2303 centimeter^{-1} and the doublet of 1302-1330 centimeter^{-1} indicate that the acetylene contains the grouping $CH_3-C\equiv C-$. The absence of the 2247 centimeter^{-1} frequency can be considered as proof that there is not formed hexyne-3 in noticeable quantity when hexadiene-1,2 is isomerized in the presence of floridin.

A visual evaluation of the spectral line intensities indicates that the hydrocarbon mixture obtained upon isomerization of hexadiene-1,2, in the presence of floridin at 230°, contains about 50% unchanged allene, 20% conjugated diene, the same of disubstituted allene, and about 10% of monosubstituted acetylene. At 280° the content of unchanged allene drops to 20% and the content of conjugated diene increases to 50%. The monosubstituted and disubstituted acetylene contents are practically unchanged.

The data obtained affirm the assumption that the formation process of the diene is not correlated with the formation process of acetylenes. Each of these transformations occurs at its own speed, and, diversely, depends upon the temperature conditions of the process.

Isomerization of hexadiene-1,2 in the presence of chromic oxide at 250° proceeds somewhat differently. Attention is drawn to the relatively high intensity of frequencies for the monosubstituted acetylene combinations, which exceeds the frequency intensity of disubstituted acetylene. It is necessary to note that in the combined dispersion spectrum of the hydrocarbon, isomerized with chromic oxide, there is, moreover, a frequency of 2094 centimeter^{-1}, the intensity of which is equal to the frequency intensity of 2125 centimeter^{-1}. This frequency points to the presence of an additional constituent. After passing one and the same portion of allene three times through a tube with chromic oxide at 250°, an intensification of the 2094 centimeter^{-1} frequency was observed. This problem was not studied in detail.

On the basis of intensity comparisons of the frequencies of the combinations, it could be assumed that the hydrocarbon formed after a single passage of the allene over chromic oxide, contained about 65% of unchanged allene, about 15% of conjugated diene, as much of the monosubstituted acetylene, and about 5% of disubstituted acetylene. The data obtained are compiled in Table 1.

TABLE 1

Catalyst	Temp. of the experiment	Content (in %)			
		Allene	Conjugated diene	Acetylene	
				Mono-substituted	Disubstituted
Floridin	230°	50	20	10	20
Floridin	280	20	50	10	20
Chromic oxide	250	65	15	15	5

Experiments with chromic oxide indicated that the initial products of allene isomerization appear to be conjugated diene and monosubstituted acetylene. The latter transforms into disubstituted acetylene. In experiments with floridin, the monosubstituted acetylene was present only in small quantity. Its main mass transformed into disubstituted acetylene.

The work of Levina, Viktorova and Eykhfeld [17], devoted to isomerization of hexyne-1 over chromic catalyst, noted the ease with which this hydrocarbon transforms. In the isomerized hydrocarbon, the authors found disubstituted acetylene and conjugated diene. Of the disubstituted acetylenes, according to their

opinion, there can be present in the mixture both hexyne-2 and hexyne-3. The latter, in particular, is affirmed by the presence in the spectrum of the frequency, 2249 centimeter $^{-1}$. The conjugated diene was demonstrated by the authors from its combination product with maleic anhydride. It was found to be hexadiene-2,4.

To determine the nature of the conjugated diene formed in our experiments, the combined dispersion spectra of a series of conjugated dienes were taken. It was found that only in the case of the hexdiene-2,4 spectrum are there intensive lines with frequencies of 1655 and 1668 centimeter $^{-1}$. Not one of the 1,3-dienes examined contained in its spectrum a line with the frequency 1668 centimeter $^{-1}$. These data are compiled in Table 2.

TABLE 2

Hydrocarbons	Frequencies of the double bonds (in cm^{-1})
$CH_2=CH-CH=CH-CH_3$	1596 (4), 1603 (4), 1646 (10), 1655 (10)
$CH_3-CH=CH-CH=CH-CH_3$	1600 (3), 1655 (10), 1668 (6)
$CH_2=C-CH=CH-CH_3$ $\quad\quad\mid$ $\quad\quad CH_3$	1605 (5), 1659 (10)
$CH_2=C-CH=C-CH_3$ $\quad\quad\mid\quad\quad\mid$ $\quad\quad CH_3\quad CH_3$	1600 (1), 1628 (5), 1645 (5), 1657 (5)
$CH_2=CH-CH=C-C_2H_5$ $\quad\quad\quad\quad\quad\mid$ $\quad\quad\quad\quad C_2H_5$	1591 (3), 1645 (10)
$CH_2=CH-C=CH-CH_3$ $\quad\quad\quad\mid$ $\quad\quad\quad CH_3$	1586 (3), 1609 (5), 1645 (10)

In Table 3 are quoted, for comparison, the combined dispersion spectra for the initial allene, the allene isomerized over floridin at 280°, and the spectrum of hexadiene-2,4. The latter was obtained by regeneration of its crystalline tetrabromide, with a m.p. of 181-182°, and boiled at 82°. As can be seen from the data in Table 3. all of the frequencies of both allene and of hexadiene-2,4 are contained in the spectrum of the isomerized hydrocarbon. Moreover, in the spectrum there is a series of frequencies corresponding to the acetylenes.

On the basis of the scheme stated, the isomerization of hexadiene-1,2 over floridin can be presented in the following manner:
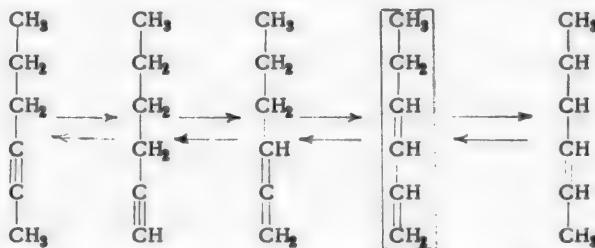
Transformation of hexadiene-1,3 into hexdiene-2,4, on floridin, proceeds very readily.

Hexadiene-1,2 was prepared by the general method worked out by Ginsburg [23].•

Hexyn-1-ol-3, required for the synthesis, was derived from dimagnesium-dibromacetylene by reaction with an equimolecular mixture of butyraldehyde and absolute alcohol [24-25]. The derived carbinol was converted into the corresponding acetylene chloride by reaction with a mixture of thionyl chloride and phosphorous oxychloride. The chloride was reduced to allene by a zinc-copper couple in absolute alcohol.

_____
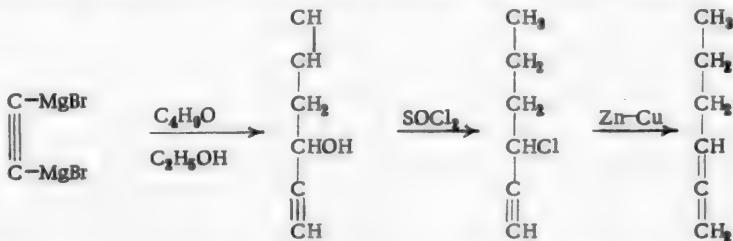
• Recently hexadiene-1,2 was synthesized [26] by an analogous method. On the basis of an infrared absorption study, the authors demonstrated that the hydrocarbon also contained some acetylenic hydrocarbon component.

TABLE 3

Hexadiene-1,2	Isomerized hydrocarbon	Hexadiene-2,4 [28]	Hexadiene-1,2	Isomerized hydrocarbon	Hexadiene-2,4 [28]
371 (2)	371 (5)		1293 (2)		
407 (1)	410 (1)			1302 (2)	1302 (6)
	435 (1)	432 (3)		1330 (1)	
	463 (1)	463 (2)		1351 (1)	
	478 (1)			1382 (5)	1376 (5)
	513 (2)		1441 (10 w)	1437 (6)	
533 (2)	538 (2)	816 (1)		1449 (6)	1449 (5)
835 (3)	833 (1)	831 (1)			1552 (1)
847 (3)	855 (1)			$1600(\frac{1}{2})$	1600 (3)
891 (2)	887 (3)			1655 (8)	1655 (10)
932 (1)		923 (1)		1668 (4)	1668 (6)
954 (2)				2123 (1)	
996 (1)	998 (1)		2234 (0)	2237 (6)	
1039 (5)	1039 (4)	1034 (3 w)		2303 (3)	
1096 (10)	1096 (2)				2858 (2)
1129 (10)	1129 (1)		2877 (3)	2872 (2)	2880 (2)
	1153 (1)	1150 (6)	2908 (3)	2917 (4)	2915 (5 w)
	1172 (1)	1167 (6)	2938 (3)	2938 (3)	
1220 (5)	1225 (1)		2990 (10)	2990 (3)	2992 (1)
	1259 (1)	1239 (8)			
		1278 (3)			

EXPERIMENTAL

Hexyne-1-ol-3. The carbinol was prepared by a general method according to Teterin and Ivanov [24].

In a three-necked round flask, equipped with reflux condenser, stirrer and dropping funnel, ethyl magnesium bromide was prepared from 60 g (2.5 mole) of magnesium and 280 g (2.5 mole) of ethyl bromide. After completion of the reaction, the dropping funnel was replaced by a gas-conducting tube, through which acetylene, from a gasometer, was slowly introduced into the flask. The acetylene was previously purified by the usual procedure, and dried with calcium chloride. The saturation time was 35–40 hours. The mixture of butyraldehyde (1.25 mole) and absolute alcohol (1.25 mole) was added to the dimagnesiumdibromacetylene formed. After standing 12 hours, the reaction mixture was poured, in a thin stream, into a flask of ice water, followed by a dilute hydrochloric acid solution until the precipitate of basic magnesium salt dissolved. The upper oily layer was separated. The water solution was extracted several times with ether. The solutions were dried over potash and distilled. The crude carbinol boiled at 135-143°. After several distillations, a fraction was separated with a b.p. of 140-141°, corresponding to hexyne-1-ol-3. Yield was 20-25% of theory.

d_4^{20} 0.8707; n_D^{19} 1.4334; MR_D 29.35; calculated 29.43.

Combined dispersion spectrum:

176 (5), 223 (2), 249 (3), 285 (3), 352 (4), 533 (2), 583 (3), 633 (3), 663 (3), 703 (2), 747 (2), 774 (2), 806 (3), 845 (2); 870 (2), 909 (5), 988 (2), 1013 (2), 1039 (3), 1068 (5), 1111 (5), 1153 (4), 1215 (3), 1295 (6), 1334 (3), 1391 (3), 1451 (8), 1642 (2), 2116 (10), 2872 (4), 2921 (5), 2968 (3).

The 1642 centimeter^{-1} frequency can be related to a double bond component. This frequency is also retained in the chloride prepared from the carbinol. It disappears upon reduction of the latter to the hydrocarbon. It is possible that it represents the added frequency of an acetylene bond, which was detected in the 1600-1700 centimeter^{-1} region of the infrared spectra of a series of acetylene alcohols and their bromides [29].

3-Chlorhexyne-1. 54 g of an equimolecular mixture of thionyl chloride and phosphorous oxychloride was placed in a flask equipped with reflux condenser. The flask was cooled with ice water. From a dropping funnel was slowly poured a mixture of 20 g of hexynol and 16 g of pyridine. After termination of reaction, the mixture was diluted with water. The chloride formed was distilled off with steam. The yield of chloride was

about 15% of theory. In the following experiments, the chlorinating mixture was diluted with 50 ml of ether. The yields of chloride increased to 50% of the theoretical. The crude chloride distilled at 60-62° (100 mm).

d_4^{20} 0.9198; n_D^{20} 1.4374; MR_D 33.19; calculated 33.09.

The combined dispersion spectrum:

178 (6), 225 (2), 269 (2), 354 (2), 453 (4), 608 (2), 648 (4), 688 (2), 730 (2), 1025 (2), 1108 (5), 1150 (2), 1170 (2), 1208 (3), 1300 (2), 1328 (2), 1441 (4), 1455 (4), 1645 (2), 2125 (10), 2877 (2), 2910 (2), 2936 (2), 2970 (2).

Hexadiene-1,2. A zinc-copper couple was first prepared. For this purpose, 60 g of zinc dust was treated several times with 3% hydrochloric acid solution, rinsed with distilled water, further treated, twice, with 2% copper sulfate solution, again rinsed several times with distilled water, then 96% alcohol, and finally with absolute alcohol. The prepared zinc-copper couple was washed down into the reaction flask with absolute alcohol.

Reaction was carried out in a three-necked round flask equipped with reflux condenser, stirrer and dropping funnel. The reflux condenser was filled with hot water and the hydrocarbon formed during the reaction, and the alcohol in part, not being condensed in the reflux, passed into a spiral coil well-cooled with ice water, to be collected in a receiver. The chloride was condensed in the hot cooler and was practically separated from the hydrocarbon fraction. 21 g of the hydrocarbon was obtained from 40 g of chloride, which amounted to about 75% of theory yield. A hexadiene-1,2 fraction was separated after several distillations over sodium, b.p. 74.4-74.8°.

d_4^{20} 0.7233; n_D^{20} 1.4269; MR_D 29.11; C_6H_{10} ? Calculated: MR_D 28.97.

The combined dispersion spectrum of the hydrocarbon is quoted in Table 3. From the data in this table it can be seen that the hydrocarbon represents almost pure allene, which contains no ethylenic hydrocarbon components. Disubstituted acetylene impurity was negligible.

Isomerization of Hexadiene-1,2. a) Isomerization over Floridin. The isomerization was carried out under the conditions described earlier by the authors. The reaction tube was of transparent quartz with a diameter of 10 mm; the length of the catalyst layer was 16 cm. The floridin was activated by the usual procedure. Temperatures of the experiments were 230 and 280°. Condensate after the tests was colorless. There was negligible amount of polymers.

The hydrocarbon isomerized at 230° distilled in a wider range (74-78°); n_D^{20} 1.4245.

The combined dispersion spectrum of the hydrocarbon isomerized at 230° differed from the combined dispersion spectrum of the hydrocarbon isomerized over floridin at 280° only by frequency intensities. Therefore we quote here a group of characteristic frequencies for allene, conjugated diene, and acetylenes:

1039 (4), 1096 (10), 1129 (8), 1655 (4), 1668 (3), 2125 (1), 2237 (5 w), 2305 (2) cm^{-1}.

The hydrocarbon isomerized at 280° was also in the form of a colorless liquid with n_D^{20} 1.4225, which boiled within a still wider range (74-82°). Negligible residue was left in the distilling flask. The combined dispersion spectrum of the hydrocarbon isomerized at 280° is given in Table 3.

b) Isomerization over Chromic Oxide. The catalyst was prepared by precipitation of chromium nitrate with ammonia [27]. The experiments were conducted in the same tube as the experiments with floridin. Temperature was 250°. The condensate, after isomerization was colorless, and distilled in the range 74-77°; n_D^{20} 1.4249. The residue in the distilling flask was negligible.

In the combined dispersion spectrum of the isomerized hydrocarbon all frequencies were detected that were observed for the hydrocarbon isomerized over floridin. In addition, there appeared a new frequency of 2094 centimeter^{-1}.

Herein is quoted a group of characteristic frequencies for allene, conjugated diene and acetylene:

1039 (5), 1096 (10), 1129 (10), 1659 (2), 2094 (1), 2116 (1), 2237 ($\frac{1}{2}$), 2305 (0) cm^{-1}.

After the same hydrocarbon sample was passed three times through a tube with chromic oxide, at 250°, the condensate was somewhat green in color. A very small quantity of polymers was found. Of all multiple combination frequencies in the combined dispersion spectrum, the most intensive was found to be the frequency of 2094 centimeter^{-1}.

SUMMARY

1. It was demonstrated that, upon contact with floridin, hexadiene-1,2 isomerizes into a hydrocarbon mixture containing allene, conjugated diene, monosubstituted diene and disubstituted acetylene.

2. The primary products of isomerization of allene are found to be the conjugated diene and the monosubstituted acetylene. The disubstituted acetylene is found to be a secondary product and is formed directly from the monosubstituted acetylene.

3. On the basis of spectroscopic data, it can be assumed that disubstituted acetylene contains as one of the substitutents the methyl group, i.e., is found to be hexyne-2.

4. The conjugated diene, formed by isomerization of hexadiene-1,2 over floridin, is found to be hexadiene-2,4.

LITERATURE CITED

[1] A. E. Favorsky, J. Russ. Chem. Soc. 19, 414, 523 (1887); 23, 283 (1891).

[2] A. E. Favorsky, The Organic Chemistry Industry, 1938, 131.

[3] G. G. Gustafson and N. Ya. Demyanov, J. prak. Chem. [2] 38, 202 (1888).

[4] Ya. M. Slobodin, J. Gen. Chem. 6, 1892 (1936).

[5] Ya. M. Slobodin, J. Gen. Chem. 5, 48 (1935).

[6] Ya. M. Slobodin, J. Gen. Chem. 4, 778 (1934).

[7] D. A. Frank-Kamenetsky and V. G. Markovich, J. Gen. Chem. 12, 619 (1942).

[8] L. M. Kucherov, J. Russ. Chem. Soc. 45, 1639 (1913).

[9] A. E. Favorsky and K. I. Debu, J. Russ. Chem. Soc. 29, 78 (1897).

[10] I. I. Ostromyslensky, Rubber and its Derivatives (1913).

[11] V. N. Ipatiev, J. Russ. Chem. Soc. 29, 75 (1897).

[12] S. V. Lebedev, J. Russ. Chem. Soc. 43, 320 (1911).

[13] German Patent 251, 216 (1912).

[14] Wislicenus. Schmidt, Ann, 313, 220 (1906).

[15] A. E. Favorsky, J. prak. Chem. [2] 44 (1891).

[16] Behal, Bl. Soc. chim (9) 49, 581 (1888).

[17] R. Ya. Levina, E. A. Victorova and V. I. Eikhfeld, J. Gen. Chem. 19, 305 (1949). *

[18] Hurd, Christ, J. Am. Chem. Soc. 59, 2161 (1937).

[19] F. O. Rays and K. K. Rays. Free Aliphatic Radicals (1935).

[20] Brackett, Pr. Nat. Acad. Sci. 14, 857 (1928).

[21] Ya. M. Slobodin, J. Gen. Chem. 7, 2376 (1937).

[22] Ya. M. Slobodin, J. Gen. Chem. 8, 1220 (1938).

[23] Ya. I. Ginsburg, J. Gen. Chem. 10, 513 (1940).

[24] Teterin and Ivanov, J. Gen. Chem. 7, 1629 (1937).

[25] Yu. S. Zalkind, J. Gen. Chem. 9, 971 (1939).

[26] Hennion, Sheehan, J. Am. Chem. Soc. 71, 1964 (1949).

[27] R. Ya. Levina and Kiryushov, J. Gen. Chem. 9, 1834 (1939).

[28] F. Tatevsky, Treshchova, Skvarchenko, Levina, J. Phys. Chem. 23, 657 (1949).

[29] J. H. Wotiz, F. A. Miller, R. J. Palchak, J. Chem. Soc. 72, 5055 (1950).

* See Consultants Bureau English translation page 265

THE INTERACTION OF α-OXIDES OF THE VINYLACETYLENE SERIES WITH OXYGEN-CONTAINING AND ORGANO-MAGNESIUM COMPOUNDS. II

F. Ya. Perveev and N. I. Kudryashova

The authors [1] established earlier that the yields of condensation products of α-oxides in the vinylacetylene series with ketones depends on the nature of the catalysts and upon the reacting ketone structure, as well as upon the structural peculiarities of the oxides. At the same time it was observed that disubstituted oxides of asymmetrical structure (I) enter into reaction with ketones and aldehydes more vigorously than the trisubstituted (II):

$$CH_2=CH-C\equiv C-\overset{\overset{\displaystyle O}{\diagup\diagdown}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_3 \qquad\qquad CH_2=CH-C\equiv C-\overset{\overset{\displaystyle O}{\diagup\diagdown}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH-CH_3$$

(I)   (II)
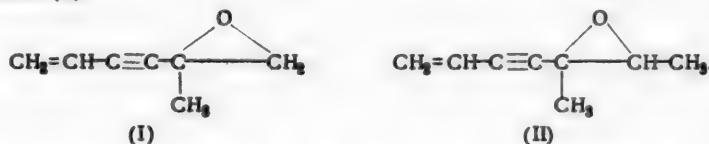
In addition, it was noticed that the more branched the chain near the carbonyl group of the reacting ketone, the smaller is the yield of condensation products—the dioxolanes.

It was of interest to clarify whether or not this dependence will be preserved upon interaction of oxides with alcohols. And, further, we have considered it necessary to investigate the influence of catalyst nature upon the yield and rate of formation of the monoethers of glycols, as well as on the order of alcohol linkage, pertaining to which subject there is but a negligible number of works.

As the subject of investigation, we took the oxides of 2-methyl-epoxy-1,2-hexenen-5-yn-3 [I] and 3-methyl-epoxy-2,3-hepten-6-yne-4 [II], and their condensations were carried out with methyl, propyl, isopropyl, n-butyl, iso-butyl, sec-hexyl and mercyl alcohols and phenol, at which time were examined the effects of alkali (NaOH and Ba(OH)$_2$) and acid catalysts (sulfuric and oxalic acids).

The interaction of oxides with alcohols in the presence of H$_2$SO$_4$ was carried out in the following manner: the oxide was added gradually to 3 times the excess of corresponding alcohol, in the presence of 2-3 drops of H$_2$SO$_4$, in such a manner that the temperature of the reaction mixture did not exceed 45°. The solution in all cases turned to a dark-brown color. After addition of excess soda, the reaction mixture was stirred to the point of complete discoloration. In the presence of oxalic acid, the oxide was added to the boiling alcohol solution, and considerably larger amount of catalyst (4-5 g) was taken.

The addition reaction of the alcohols to α-oxides of the vinylacetylene series goes very rapidly in the presence of sulfuric acid, and with large heat evolution; reaction is practically terminated within 15-17 minutes. The disubstituted oxide of asymmetrical structure (I) reacts with alcohols more vigorously than the oxide (II). A very noticeable difference in the rate of alcohol addition is observed when alkaline catalysts are present. Thus, for example, upon interaction of oxide (I) with methyl alcohol, reaction was terminated at 3.5 hours, with a yield of 73%, while at the same time, in the case of oxide (II) reaction did not end (some non-reacted oxide remained) even after 35-40 hours of heating, and the yield of condensation products reached only 30%.

In the case of alkaline catalysts, the synthesis of glycol monoethers was carried out in the following manner: 0.4 g of metallic Na, or 0.8 g of NaOH, or 1 g of Ba(OH)$_2$ was added to 1 mole of the corresponding alcohol. The solution was heated in a round-bottomed flask with a reflux condenser to 60-80°, and into it was poured the oxide.

The glycol monoethers are represented by colorless, mobile, liquids, with a weak, almost non-characteristic odor, with the exception of the methyl ether oxide of 3-methyl-epoxy-2,3-hepten-6-yn-4, which possessed a faint, pleasant odor. The monoethers become yellow on standing in air in the absence of antioxidants, and gradually polymerize, forming viscous, gummy liquids, which, over a period of 1.5-2 months, transform into a hard, vitreous

No.	Catalyst	Formula	B.p.	n_D^{20}	d_4^{20}	MR$_D$ found	calc.	Yield (%)
1	H$_2$SO$_4$ (COOH)$_2$	CH$_2$=CH-C≡C-C(CH$_3$)(OCH$_3$)CH$_2$OH	76-77 (4 mm)	1.4860	0.9840	40.9	39.8	81
2	Na, NaOH	CH$_2$=CH-C≡C-C(CH$_3$)(OH)CH$_2$OCH$_3$	69-70 (3 mm)	1.4802	0.9644	41.3	39.8	73
3	(COOH)$_2$	CH$_2$=CH-C≡C-C(CH$_3$)(OC$_3$H$_7$)CH$_2$OH	93-95 (7 mm)	1.4764	0.9430	50.4	49.2	58
4	Na	CH$_2$=CH-C≡C-C(CH$_3$)(OH)CH$_2$OC$_3$H$_7$	91-92 (7 mm)	1.4691	0.9280	50.5	49.2	63
5	H$_2$SO$_4$	CH$_2$=CH-C≡C-C(CH$_3$)(OC$_4$H$_9$)CH$_2$OH	94-95 (3 mm)	1.4748	0.9304	55.0	53.7	79
6	Na	CH$_2$=CH-C≡C-C(CH$_3$)(OH)CH$_2$OC$_4$H$_9$	89-90 (3 mm)	1.4680	0.9190	55.1	53.7	24
7	H$_2$SO$_4$	CH$_2$=CH-C≡C-C(CH$_3$)(iso-OC$_4$H$_9$)CH$_2$OH	90-91 (5 mm)	1.4713	0.9235	55.2	53.7	64
8	H$_2$SO$_4$	CH$_2$=CH-C≡C-C(CH$_3$)(OC$_6$H$_{13}$)CH$_2$OH	100-101 (3 mm)	1.4703	0.9126	64.3	62.9	65
9	H$_2$SO$_4$	CH$_2$=CH-C≡C-C(CH$_3$)(OCH$_3$)CHOH(CH$_3$)	75-76 (5 mm)	1.4811	0.9600	45.4	44.3	69-70
10	Na	CH$_2$=CH-C≡C-C(CH$_3$)(OH)CH(OCH$_3$)CH$_3$	74-78 (8 mm)	1.4754	0.9543	45.5	44.3	30
11	(COOH)$_2$	CH$_2$=CH-C≡C-C(CH$_3$)(OC$_3$H$_7$)CHOHCH$_3$	96-98 (10 mm)	1.4736	0.9283	55.1	53.6	48
12	H$_2$SO$_4$ (COOH)$_2$	CH$_2$=CH-C≡C-C(CH$_3$)(iso-OC$_3$H$_7$)CHOHCH$_3$	72-73 (3 mm)	1.4709	0.9225	55.2	53.6	58
13	H$_2$SO$_4$	CH$_2$=CH-C≡C-C(CH$_3$)(OC$_4$H$_9$)CHOHCH$_3$	95-96 (3 mm)	1.4700	0.9195	59.5	58.3	58

mass. The pure monoethers distill in the absence of air with a little resinification. The resinous products remaining after distilling, exploded upon heating over 140°.

The physical constants and monoether yields are given in the table

In the presence of acid catalysts, as is shown in the table, the monoether is formed, which possesses a higher boiling temperature, greater specific gravity and index of refraction, as compared with the monoether obtained with alkaline catalyst. On this basis we can assert that with acid catalysts the tertiary monoether is formed in all cases, with the alkaline— the primary (with 2-methyl-epoxy-1,2-hexen-5-yne-3) and the secondary (with 3-methyl-epoxy-2,3-heptene-6-yn-4). A. A. Petrov [2] observed a similar interaction of alcohols with propylene oxide.

It might be assumed that the formation of isomeric monoether mixtures is possible in the first instance To prove the identity of the products obtained, certain synthesized monoethers were carefully fractionated, and those fractions boiling within an interval of a few degrees possessed the same index of refraction and specific gravity. For example, the methyl ether, obtained from the oxide (I), boiled at 74-77° (4 mm), n_D^{20} 1.4860, d_4^{20} 0.9840 and 77-78° (4 mm), n_D^{20} 1.4859, d_4^{20} 0.9847. The propyl ether, obtained from oxide (II), boiled at 96-98° (10 mm), n_D^{17} 1.4736, d_4^{17} 0.9283 and 98-101° (10 mm), n_D^{17} 1.4736, d_4^{17} 0.9280, while the differences in refractive indices and specific gravity is very considerable between the primary and tertiary monoethers. For example: the methyl ether, obtained from the oxide in the presence of H$_2$SO$_4$, has n_D^{20} 1.4860 d_4^{20} 0.9840, and the methyl ether from the same oxide, obtained by the alkaline method, has n_D^{20} 1.4802, d_4^{20} 0.9644.

On the basis of the data obtained, it can be concluded that the rate of formation and the yield of monoethers depends on the oxide structure, on the nature of the catalyst, and on the structure of the reacting alcohol. The disubstituted (2-methyl-epoxy-1,2-hexene-5-yn -3) oxides react more vigorously and give greater yield of condensation products, than the trisubstituted (3-methyl-epoxy-2,3-heptene-6- yn -4).

In the presence of sulfuric acid, the increase in chain length of the reacting alcohol has an almost unnoticeable effect upon the yield of monoether. A chain branching near the hydroxyl group shows noticeable influence. Thus, for example: n-butyl and isobutyl ethers of the oxide (I) are obtained with yields, respectively, of 79 and 64%, and ter-butyl alcohol, in the presence of oxalic acid, does not enter into reaction with this oxide at all.

In the presence of alkaline catalyst, an increase in chain length, or branching near the hydroxyl group of the reacting alcohol, sharply decreases the yield of monoether. This evidently is in full accord with the concept that, with an increase in the chain of the corresponding alcohol, or in its branching, the acidity of the hydrogen atom of the hydroxyl group decreases. Thus, for example, upon interacting the oxide (I) with methyl alcohol in the presence of alkaline catalyst, the reaction product yield reaches 81%, while the yield of condensation product of the given oxide with n-butyl alcohol, under the same conditions, does not exceed 24%.

The reaction of phenol with oxide (I) starts and proceeds with considerable evolution of heat when heated above 60° in the presence of alkaline catalyst. In order to avoid an explosion, the oxide must be added gradually to the phenolate, heated to 60°.

The interaction speed of the alcohols with a-oxides of the vinylacetylene series changes, depending upon the nature of the alkaline catalyst. Thus, for example, with methyl alcohol, in the presence of NaOH, the reaction is complete in 4 hours, and the yield of monoether reaches 68%, while with $Ba(OH)_2$ under the same conditions, there remains some unreacted oxide, and the monoether glycol does not exceed 30%. Upon reaction with acid catalysts, the break in the oxide ring occurs at the carbon attached directly to the triple bond, i.e., the formation of tertiary monoethers occurs. In the presence of alkaline catalyst, the order of linkage is reversed.

EXPERIMENTAL

1. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn- 3 with methyl alcohol in the presence of H_2SO_4. 50 ml of methyl alcohol and 1 drop of H_2SO_4 were placed in a round-bottomed flask with mechanical stirrer and reflux condenser. 15 g of the oxide was gradually added to avoid an increase in temperature over 50° in the reaction mixture. The solution turned dark brown in color. An excess of soda was added to the reaction mixture after 10-15 minutes. The stirring was continued until the coloration had disappeared. The soda was then filtered off, and the excess alcohol removed. The substance obtained was distilled in vacuo (Formula 1 in the table).

0.1167, 0.1031 g substance: 19.0, 16.9 ml CH_4 (11°, 760.6 mm). 0.1059 g substance: 0.2655 g CO_2, 0.0832 g H_2O. Found %: active H 0.697, 0.702; C68.38; H 8.79. $C_8H_{12}O_2$. Calculated %: active H 0.719; C 68.54; H 8.63.

2. Interaction of 2-methyl-epoxy-1,2-hexen-5-yne- 3 (I) with propyl alcohol in the presence of oxalic acid. To 100 ml of propyl alcohol and 2 g of oxalic acid, was gradually added, with stirring, 39 g of the oxide in such a manner that the temperature of the reaction mixture did not rise above 55°; After addition of oxide, the reaction mixture was heated on a water bath at 80° for 10 minutes. The propyl alcohol excess was partially removed, and the remaining yellowish product washed several times with water, dried with Na_2SO_4 and distilled in vacuo (Formula 3 in the table).

0.1102, 0.1211 g substance: 16.1, 17.7 ml CH_4 (15°, 766.4 mm). 0.0900 g substance: 0.2342 g CO_2, 0.0840 g H_2O. Found %: active H 0.619, 0.621; C 71.13; H 9.24. $C_{10}H_{16}O_2$. Calculated %: active H 0.603; C 71.39; H 8.99.

3. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with n-butyl alcohol in the presence of H_2SO_4. 20 g of the monoether was obtained from 15 g of the oxide, the constants of which are given in the table (Formula 5).

0.1151, 0.1133 g substance: 15.7, 15.4 ml CH_4 (13.5°, 762.6 mm). 0.1082 g substance: 0.2861 g CO_2, 0.0971 g H_2O. Found %: active H 0.579, 0.577; C 72.35; H 10.04. $C_{11}H_{18}O_2$. Calculated %: active H 0.553; C 72.49; H 9.96.

4. Interaction of 2-methyl-epoxy-1,2-hexene-5-yn-3 (I) with sec-hexyl alcohol in the presence of H_2SO_4. 19 g of the monoether was obtained from 15 g of the oxide, its constants being given in the table (Formula 8).

0.1160, 0.1406 g substance: 14.7, 16.9 ml CH_4 (14.5°, 752.2 mm). 0.1102 g substance: 0.2993 g CO_2; 0.1055 g H_2O. Found %: active H 0.508, 0.501; C 74.12; H 10.71. $C_{13}H_{22}O_2$. Calculated %: active H 0.479; C 74.24; H 10.54.

5. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with isobutyl alcohol in the presence of H_2SO_4. 16 g of the monoether was obtained from 15 g of the oxide (Formula 7 in the table).

0.1326, 0.1121 g substance: 17.6, 15.2 ml CH_4 (12°, 757.9 mm). 0.1038 g substance: 0.2749 g CO_2. 0.0939 g H_2O. Found %: active H 0.564, 0.576; C 72.27; H 10.12. $C_{11}H_{18}O_2$. Calculated %: active H 0.553; C 72.49; H 9.96.

6. Interaction of 2-methyl-opoxy-1,2-hexen-5-yne-3 with methyl alcohol in the presence of Na methylate. 1 mole (32 g) of methyl alcohol and 0.4 g of metallic Na was placed in a round-bottomed flask with a reflux condenser. The solution was heated to boiling, and 20 g of oxide then added to it. The heating was then continued for about 4 hours until the oxide odor disappeared. The methyl alcohol excess was then distilled off in vacuo. The remaining viscous mass was washed with water and extracted with ether. The ether solution was dried with Na_2SO_4, the ether removed and the product obtained fractionally distilled in vacuo. 15 g of monoether was isolated (Formula 2 in the table).

0.1379, 0.0918 g substance: 22.9, 15.8 ml CH_4 (14°, 758.3 mm) 0.1121 g substance: 0.2795 g CO_2, 0.0887 g H_2O. Found %: active H 0.700, 0.725; C 68.21; H 8.85. $C_8H_{12}O_2$. Calculated %: active H 0.719; C 68.54; H 8.63.

7. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with methyl alcohol in the presence of NaOH. 1 mole of methyl alcohol, 0.8 g NaOH and 15 g of the oxide were placed in a round-bottomed flask. The reaction mixture was heated for 4 hours. 13 g (68%) of the monoether was isolated with a b.p. 74-75° (5 mm), n_D^{20} 1.4800.

8. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 with isopropyl alcohol in the presence of Na alcoholate. 1 mole of propyl alcohol, 0.4 g of Na and 15 g of the oxide were taken. 14.5 g of the monoether (Formula 4 in the table) was obtained.

0.1280 g substance: 19.2 ml CH_4 (13.5°, 748.3 mm). 0.1254 g substance: 18.9 ml CH_4 (13.5°; 752.2 mm). 0.1058 g substance: 0.2759 g CO_2, 0.0952 g H_2O. Found %: active H 0.625, 0.628; C 71.15; H 9.18. $C_{10}H_{16}O_2$. Calculated %: active H 0.603; C 71.39; H 8.99.

9. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with n-butyl alcohol in the presence of Na alcoholate. 20 g of the oxide, 0.5 mole of n-butyl alcohol, 0.2 g of Na were taken. The mixture was heated for 4 hours at 70-80°. 8 g of the monoether (Formula 6 in the table) was obtained.

0.1242, 0.1334 g substance: 16.5, 17.8 ml CH_4 (13°, 752.2 mm). 0.1018 g substance: 0.2700 g CO_2, 0.0994 g H_2O. Found %: active H 0.558, 0.560; C 72.38; H 10.16. $C_{11}H_{18}O_2$. Calculated %: active H 0.553; C 72.49; H 9.96.

10. Interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with methyl alcohol in the presence of $Ba(OH)_2$. 15 g of the oxide, 1 mole of methyl alcohol and 1 g of $Ba(OH)_2$ were taken. The reaction mixture was heated to boiling for 4 hours. 7 g (37%) of monoether with b.p. 74-75° was isolated, n_D^{20} 1.4802, d_4^{20} 0.9642 and a low fraction — non-reacted oxide with n_D^{20} 1.4780.

11. Interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4 (II) with methyl alcohol in presence of H_2SO_4. 40 ml of methyl alcohol and 5 drops of H_2SO_4 were placed in a round-bottomed flask with mechanical stirrer and reflux condenser. 15 g of the oxide was added gradually in a manner to avoid increase in temperature above that of 45°. 16.5 g of the monoether was isolated (Formula 9 in the table).

0.1091, 0.1339 g substance: 17.1, 21.1 ml CH_4 (16°, 752.5 mm). 0.1182 g substance: 0.3029 g CO_2, 0.1067 g H_2O. Found %: active H 0.649, 0.653; C 69.92; H 9.21. $C_9H_{14}O_2$. Calculated %: active H 0.655; C 70.10; H 9.15.

12. **Interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4** (II) with propyl alcohol in the presence of oxalic acid. A mixture of 50 ml propyl alcohol and 6 g of oxalic acid was heated to boiling, 25 g of the oxide added dropwise over 15 minutes. A noticeable evolution of heat was observed. After addition of the oxide, the reaction mixture was again heated for 10-15 minutes. The alcohol was then partially distilled off, the remaining mass distilled with water, dried with Na_2SO_4 and redistilled in vacuo. 15 g of the monoether was isolated (Formula 11, in the table).

0.1014, 0.1204 g substance: 14.0, 16.3 ml CH_4 (16.5°, 763.5 mm). 0.1004 g substance: 0.2672 g CO_2, 0.0891 g H_2O. Found %: active H 0.579, 0.568; C 72.59; H 9.93, $C_{11}H_{18}O_2$. Calculated %: active H 0.553; C 72.49; H 9.95.

13. **Interaction of 3-methyl-epoxy-2,3-hepten-6-yne-4** (II) with isopropyl alcohol in the presence of H_2SO_4. To 50 ml of isopropyl alcohol in the presence of 3 drops H_2SO_4, 15 g of the oxide was gradually added; the reaction mixture temperature rose to 35°. 13 g (Formula 12 in the table) was isolated.

0.1261 g substance: 16.8 ml CH_4 (16°, 752.5 mm). 0.1081 g substance: 0.2865 g CO_2, 0.1060 g H_2O. Found %: active H 0.565, 0.572; C 72.31; H 10.01. $C_{11}H_{18}O_2$. Calculated %: active H 0.553; C 72.49; H 9.95.

14. **Interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4** (II) with isopropyl alcohol in the presence of oxalic acid. A mixture of 50 ml isopropyl alcohol and 5 g of oxalic acid was heated to 70°, and 25 g of the oxide added to it. 10 g of the monoether was obtained with a b.p. of 74-75° (3 mm); n_D^{18} 1.4709; d_4^{18} 0.9229.

15. **Interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4** (II) with n-butyl alcohol in the presence of H_2SO_4. 14 g of the monoether was obtained from 15 g of the oxide (Formula 13 in the table).

0.1564, 0.1217 g substance: 19.4, 15.2 ml CH_4 (15°, 757.1 mm). 0.1121 g substance: 0.3010 g CO_2, 0.1137 g H_2O. Found %: active H 0.521, 0.525; C 73.27; H 10.35. $C_{12}H_{20}O_2$. Calculated %: active H 0.514; C 73.42; H 10.27.

16. **Interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4** (II) with methyl alcohol in the presence of Na methylate. 1 mole (32 g) of methyl alcohol and 0.4 g of Na were placed in a round-bottomed flask with a reflux condenser, and 15 g of the oxide was added to the boiling solution. The reaction mixture was heated at boiling alcohol temperature for 35-40 hours. The alcohol excess was then driven off, and the remaining thick mass was washed with water, extracted with ether, dried with Na_2SO_4 and redistilled in vacuo. 6 g of the monoether was obtained (Formula 10 in the table). 0.111 g sub.: 17.3 ml CH_4 (13°, 748.3 mm). Found %: active H 0.650. Calculated %: active H 0.655.

17. **Interaction of 2-methyl-epoxy-1,2-hexene-5-yn-3** (I) with phenol in the presence of Na phenolate. 0.3 g of metallic sodium was added to 20 g of phenol at 60°, and 15 g of the oxide was then added gradually; heat evolution was then observed. The addition of oxide was regulated in such a manner as to avoid raising the temp. of the reaction mixture to more than 80-90°. After addition of the oxide, the solution was heated for 30 minutes at 80-90°. The excess phenol was washed out with alkali. The upper layer was removed and the aqueous layer extracted with ether. 18 g of crude viscous product was isolated. The authors were not able to determine its physical constants, because at a temperature over 140° and 1 mm it decomposed.

SUMMARY

1. Upon interaction of 2-methyl-epoxy-1,2-hexen-5-yn-3 (I) with alcohols in the presence of sulfuric acid and oxalic acid, the tertiary monoethers of glycol derivatives of methyl, propyl, n-butyl, isobutyl and hexyl alcohols were isolated.

2. Upon interaction of 3-methyl-epoxy-2,3-hepten-6-yn-4 (II) with alcohols in the presence of the above-indicated reagents, monoethers were obtained — derivatives of methyl, isopropyl, propyl and n-butyl alcohols.

3. Upon interaction of 2-methyl-epoxy-1,2-hexen-5-yne-3 and 3-methyl-epoxy-2,3-heptene-6-yn-4 with alcohols, in the presence of alkaline catalysts (Na alcoholate, NaOH, $Ba(OH)_2$) there separated, respectively, the primary and secondary monoether derivatives of methyl, propyl and n-butyl alcohols.

4. It was determined that the formation of tertiary monoethers of glycols is only realized under the influence of acid catalysts, and in the presence of alkaline catalysts there is formed the primary monoether for 2-methyl-epoxy-1,2-hexen-5-yn-3- and the secondary for 3-methyl-epoxy-2,3-hepten-6-yn-4.

The thermal decomposition of styrene oxide, and also its condensation with ammonia, were conducted in an apparatus described in the preceding works [1, 2, 4], with the only difference that styrene oxide was added from a buret into the vaporizer, which was heated by an oil bath at 260°, and from here the gaseous styrene oxide passed into the reaction tube.

The styrene oxide was obtained by the method of Fourneau [6] from styrene, using iodine and mercury oxide in ether medium, except that in the last phase of conversion of the iodohydrin into the oxide, alcohol was substituted for ether. To make the point clear, to obtain styrene oxide from iodohydrin in ether medium with the aid of powdered caustic potash, requires, in contrast to the method we describe, not 1-2 days, but 6-7 days at 5-6 times the excess of alkali and stirring of the reaction mass.

The styrene oxide has the following constants: b.p. 190-192° at 747 mm; b.p. 91-94° at 30 mm; d^{21} 1.0120, which coincides with the literature data [6].

1. Thermal Decomposition of Styrene Oxide at 500°. Volume rate of the oxide was 40-42. 72 g was taken for the experiment. The experiment duration was 4 hours. 3 ml of water and 59 ml of oily condensate and 6 liters of gas were obtained.

The oily condensate was washed with 20 ml of 0.1 normal NaOH. The separated alkaline solution, together with water, obtained from the condensation, was carefully steamed off. The residue was dissolved in a small volume of water and acidified with hydrochloric acid; at which time crystals of benzoic acid precipitated, which, after recrystallization, melted at 120-122°, and did not give a depression with benzoic acid.

The oily condensate was dried with calcium chloride and was fractionally distilled from a Favorsky flask. After a few distillations, the following fractions were successfully separated: 1) 75-112° 2.4 g, 2) 130-150°,10.0 g, 3) 170-180°, 4.0 g, 4) 187-197°, 6.0 g, 5) 200-203°,15.0 g, 6) 300-340°,2.7 g.

The first fraction consisted of benzene and toluene, the presence of which was proved by nitration and testing with powdered KOH in petroleum ether [7]. Then was observed a turquoise coloration of the upper part of the alkali and after 1-1.5 minutes an orange-yellow coloration in the lower part, which pointed to the presence of benzene and toluene. 1.5 g of this fraction was oxidized with potassium permanganate, and the non-oxidized liquid was nitrated by a nitration mixture at 100-110°. As a result, dinitrobenzene was obtained, which, after recrystallization from alcohol, had an m.p. of 88° (90° according to the literature data [15]).

From the 2nd fraction was separated, by treatment with bromine water, dibromstyrene, with m.p. 70-71°, which did not give depression upon mixed test (in the literature are cited m.p. 69° [8] and 72-73° [9].).

The residue fraction, after separation of the dibromstyrene, was treated several times with small volumes of sulfuric acid, washed with water and soda, dried with calcium chloride and distilled. In this way, 3 g of ethylbenzene was separated, which had a b.p. of 134-136°; d_4^{20} 0.8650 (according to the literature data [9] the b.p. is 135.8-136.3°; d_4^{20} 0.8664.

From the 3rd fraction benzaldehyde was separated through the bisulfite derivative, and from it the same benzaldehyde by soda solution, which upon standing oxidized easily to benzoic acid with m.p. 121°.

From the 4th fraction the same bisulfite derivative was obtained (in the amount of 3.4 g). After recrystallization from water-alcohol solution, and drying in a vacuum dessicator, the per cent sulfur in it was determined, which corresponded to the bisulfite derivative of phenylacetaldehyde.

0.2314 g substance: 0.2373 g $BaSO_4$. Found %: S 14.11. $C_7H_9O_4SNa$. Calculated %: S 14.28.

The 5th fraction represented almost pure acetophenone, for which was obtained the oxime, with m.p. 59° [11, 15], and from it, by Beckmann rearrangement, acetanilide with m.p. 110-112°, which corresponds exactly with the literature data [15].

The 6th fraction was once more distilled under vacuum (b.p. 220-230° at 20 mm), and from it was obtained the semicarbazone with m.p. 150° after recrystallization from benzene, which corresponds to the melting point of dypnone semicarbazone (151° according to the literature data [13]).

2. Condensation of Styrene Oxide with Ammonia over Alumina. The styrene oxide and ammonia were taken in the molar ratio of 3:1. 72 g of styrene oxide was taken in all; the volume rate was 40-42; the time during which the condensation was conducted was 4 hours and 40 minutes. 53.5 g of condensate and 5200 ml of

gas were obtained in all. Upon fractional distillation, the following fractions were separated: 1) 75-120°, 3.0 g, 2) 120-150°, 6.2 g, 3) 150-180°, 1.7 g, 4) 180-197°, 4.3 g, 5) 197-205°, 24.7 g, 6) 205-260°, 8.0 g, 7) 260-285°, 3.0 g, 8) 285-340°, 1.5 g. 52.4 g of liquid fraction was thus obtained which comprised 72.8% in terms of styrene oxide taken.

In the first fraction were found nitrogen-containing compounds of the pyrrole series (coloring pine splinter treated with vapors of hydrochloric acid). To remove pyrrole compounds in this fraction, gaseous hydrogen chloride was passed through; at which the liquid turned red, and after a given time a precipitate of dark-red resinous substance settled to the bottom of the tube, which was separated from the liquid. The liquid was further treated with a concentrated solution of alkali, and the alkaline solution separated and extracted with ether. The ether extract was mixed with that layer which did not dissolve in alkali, and by fractional precipitation with picric acid, followed by recrystallization from acetone, there was obtained the picrate with m.p. 163°, which did not produce significant depression with the known picrate of pyridine. Thus, among the nitrogen-containing compounds of this fraction is included pyridine.

The subsequent fractions with b.p.'s from 120 to 260° (i.e., the 2nd, 3rd, 4th, 5th and 6th) do not contain nitrogen, and basically represent the same substances which were obtained by thermal decomposition of styrene oxide over alumina at 500° (see above-studied experiment). Thus, the 5th fraction was found to be benzaldehyde, the 6th acetophenone, and so forth.

The fraction with b.p. 260-285° contained nitrogen, and from it was separated a picrate with m.p. 149-152°, which, after 4 recrystallization from acetone, had an m.p. of 158-160°. The determination of nitrogen in the picrate (by the semimicro method):

0.202 g substance: 2.64 ml N_2 (21.5°, 733 mm). Found %: N 14.33. $C_{12}H_{11}N \cdot C_6H_3N_3O_7$. Calculated %: N 14.07.

From the analysis we concluded that the picrate corresponds to methylphenylpyridine, but we did not succeed in solving the problem of its structure.

From the same fraction after previous treatment with hydrogen chloride (at which time there separated a little of the red-colored tar) there was obtained a platinate, which after recrystallization from hot water, had an m.p. of 198-200° (with decomposition). After drying in a vacuum dessicator over phosphoric anhydride for 24 hours, the platinum percentage in it was determined for which precipitate an ignition time of 12 hours was required; since the platinate contains a large amount of carbon which is adsorbed by the platinum and burns out with difficulty, this leads to too high a platinum content.

0.3113 g substance; 0.0825 g Pt. Found %. Pt 26.51. $(C_{12}H_{11}NHCl)_2 PtCl_4$. Calculated %: Pt 26.06.

Analysis of the gas was conducted in the usual way in the VTI apparatus. In the gases were found: CO_2 3.2%; C_nH_{2n} 21%; O_2 0.3%; CO 8.7%; H_2 35%; C_nH_{2n+2} 31%.

Moreover, there was determined acetaldehyde [16] and formaldehyde [16] in the gases before their entrance into the gasometer, proven by qualitative tests.

SUMMARY

1. The thermal decomposition of styrene oxide over aluminum oxide was investigated at 500°, and there were obtained as the basic products of the reaction, besides acetophenone — the aromatic hydrocarbons styrene, ethylbenzene, toluene and benzene, and the aromatic aldehydes benzaldehyde and phenylacetic aldehyde.

2. The condensation of styrene oxide (under the above-indicated conditions) was investigated, in the presence of ammonia. In this case the formation of nitrogen-containing heterocylic compounds was established, among which were demonstrated pyridine, methylphenylpyridine (of undetermined structure) and derivatives of pyrrole.

LITERATURE CITED

[1] M.S. Malinovsky and B. N. Moryganov. J. Appl. Chem. 20, 630 (1947).

[2] M.S. Malinovsky, Scientific Reports of Gorky State Univ. 15, 103 (1949).

[3] Yu. K. Yuryev, K. Yu. Novitsky, E. Mingulina, Proc. Acad. Sci. U.S.S.R. 74, 87 (1950).

[4] M.S. Malinovsky and S. N. Baranov, J. Appl. Chem. *   25, 410 (1952).

[5] A.E. Chichibabin, M.P. Oparina, J. Russ. Phys. Chem. Soc. 54, 601 (1924).

[6] E. Fourneau, M. Tiffeneau, comptes. rend. 140, 1595 (1905).

[7] T. Eydus and T. Fedichkina, Bull. Acad. Sci. U.S.S.R., 1940, No. 2, 275.

[8] P. Ferko, Ber., 20, 661 (1887).

[9] S. R. Sergienko, Proc. Acad. Sci. U.S.S.R. 29, 37 (1940).

[10] K. Rosenmund, F. Zetz, Ber., 54, 432 (1921).

[11] A. Janny, Ber., 15, 2781 (1882).

[12] E. Beckmann, Ber., 20, 1509 (1887).

[13] A. Courtot, Bl. Soc. chim. (3), 35, 356 (1906).

[14] K. Josephson, Ber., 56, 1771 (1923).

[15] G.T. Clark, Manual for Qualitative and Quantitative Organic Analysis. Kharkov-Kiev (1934).

[16] G. Meier, Analysis and Determination of Organic Compounds. Leningrad. (1937).

REACTIONS OF THE METHYL ESTER OF METHACRYLIC ACID
## WITH ORGANO-MAGNESIUM COMPOUNDS

I. REACTION OF METHYLMETHACRYLATE WITH ISOPROPYLMAGNESIUM BROMIDE

A. I. Lebedeva and E. D. Vainrub

A. E. Favorsky and A. I. Lebedeva investigated the reaction of sulfuric acid with dimethylvinylcarbinol [1] and separated from the mixture obtained at that time several products, among them linalool and geraniol. In the present work we have considered an investigation of the reaction of sulfuric acid and certain other reagents with diisopropylisopropenylcarbinol, where we decided to obtain the latter from the methyl ester of methacrylic acid and isopropylmagnesium bromide. We assumed that the homolog of linalool synthesized in this manner, containing the isopropyl radicals, will possess an entirely different odor and be applied in the perfume industry. However, after carrying out the usual organo-magnesium synthesis, with decomposition of the obtained organo-magnesium complex with water and ice, we obtained mainly a liquid product, with b.p. 108-109° at 4 mm, which contained neither hydroxyl nor carbonyl, and did not react with a water solution of permanganate or with bromine water. A determination of the elementary composition, molecular weight and molecular refraction, has indicated that we obtained the compound corresponding to the formula $C_{13}H_{24}O_4$. Upon saponification of this compound with alcoholic alkali there was obtained a crystalline saturated acid, with an m.p. of 124-125° which, according to the analysis data, corresponded to the formula $C_{11}H_{20}O_4$. The determination of molecular weight, acid equivalent and percentage content of silver in the silver salt of this acid has indicated that the acid obtained by the authors is dibasic, and upon heating easily splits off water and transforms into the anhydride with an m.p. of 73-74°, corresponding to the formula $C_{11}H_{18}O_3$. Upon heating the anhydride with alkali solution it transforms easily into sodium or potassium salt of the acid. Half of the potassium salt was converted into the silver salt and analyzed for the silver content, whereupon the silver content corresponded to the initial acid, the second half of the potassium salt was converted into the original acid. Such ease of anhydride formation is intrinsic only to succinic and glutaric acids, and to their saturated fatty dibasic acid derivatives, which allowed the assumption that a derivative of glutaric acid is formed when conducting the organomagnesium synthesis. K. A. Oglobin [2] obtained a mixture of dimethylisopropenylcarbinol and methyl-sec-butylketone upon reaction of ethylmagnesium bromide with the methyl ester of methacrylic acid under analogous conditions. Upon substituting methyl for the isopropyl, the direction of the reaction might be easily altered. It is known, for example, that it is impossible to obtain the tertiary alcohol upon reaction of isopropylbromide with diisopropylketone in the presence of magnesium [3]. Evidently in our case the linkage of isopropylmagnesium bromide occurs in position 1,4. The transformations indicated can be presented by the following scheme:

$$\longrightarrow \quad \begin{array}{c} H_3C \\ \\ H_3C \end{array} CHCH_2C\underset{O^2}{\overset{CH_3}{\underset{|}{C}}}CH_2\overset{CH_3}{\underset{|}{C}}HC\overset{O}{\underset{OCH_3}{\diagdown}} \\ \underset{OCH_3}{\overset{|}{C}} \\ \text{(IV)}$$

$$\underset{CH_3}{\overset{CH_3}{CH_3CHCH_2}}\underset{COOH}{\overset{CH_3}{C}}CH_2\overset{CH_3}{CHCOOH} \longrightarrow CH_3CHCH_2\overset{CH_3}{\underset{OC}{C}}\underset{O}{\overset{CH_2}{\diagup}}\underset{CO}{CHCH_3}$$

$$\text{(V)} \qquad\qquad\qquad \text{(VI)}$$
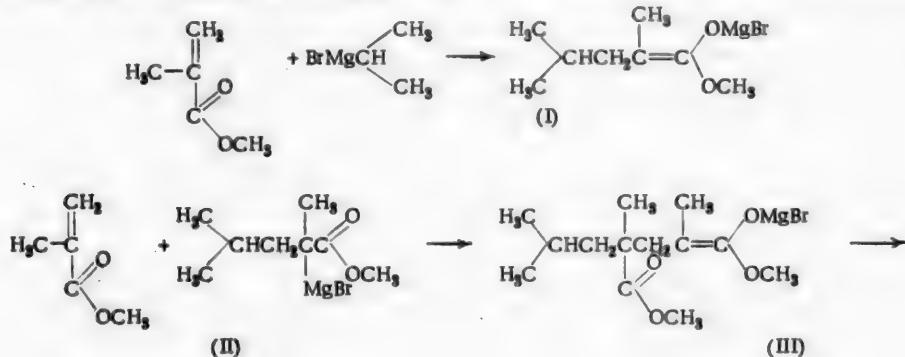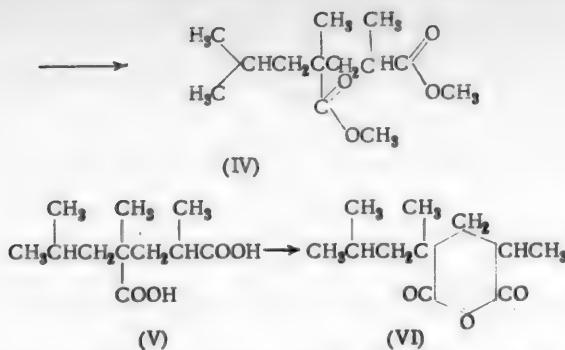
The obtained unsaturated organomagnesium complex (I) isomerizes to the saturated compound (II), and links anew to the second molecule of methyl methacrylate, with the formation of the enol form of the ester of the dibasic acid (III). Upon decomposition of the organomagnesium complex with water, there is formed the dimethyl ester of a,d-dimethyl-a-isobutylglutaric acid (IV). By saponfication of the ester by alkali, there is obtained the free dibasic saturated a,a',-dimethyl-a-isobutyl-glutaric acid (V). The authors have tried to de-carboxylate the acid obtained, using the thermal method according to Vogel [4], but instead of the expected hydrocarbon, they have obtained the anhydride of the acid (VI), which distills without decomposition at 287-289°, and melts at 73-74° after recrystallization from petroleum ether (45-75°).

Upon reaction of magnesium phenylbromide with the methyl ester of cinnamic acid (at -10°), Kohler [5] obtained the methyl ester of β,β-diphenylpropionic acid and diphenylpropiophenone. Kohler considered that these products are formed as a result of addition of phenyl-magnesium bromide to the methyl ester of cinnamic acid in position 1,4. At first there evidently occurs addition of one molecule of magnesium phenyl-bromide, as is quoted in the scheme of A.D. Petrov and P.S. Bataeva [6], with the formation of the methyl ester of β,β-diphenylpropionic acid. However, the reaction may not be terminated at this point only. Petrov and Bataev, investigating the interaction of esters of cinnamic acid with phenylmagnesiumbromide at +20°, have demonstrated that the only reaction product is the saturated 1,1,3,3-tetraphenylpropyl alcohol. The authors have come to the conclusion that termination of the intermediate reaction stage may be conditioned not only by spatial interference, but also by decrease in the temperature of the experiment.

EXPERIMENTAL

Synthesis of the Dimethyl ester of Dimethylisobutylglutaric acid. To 6.5 g of magnesium (in powder form) was added, dropwise, with stirring, 31 g of isopropylbromide in 75 ml of absolute ether. After dissolution of the magnesium, the mixture was stirred for an additional two hours at room temperature, and then cooled on the outside with water and ice, and 13 g of the methylester of methacrylic acid in 25 ml of ether was added dropwise. On the following day the organic magnesium complex was decomposed with water and ice. The ether layer was separated. The remaining residue was decomposed with ice and dilute hydrochloric acid. The solution was treated with ether after the basic salts of magnesium were dissolved. The ether extraction was washed with soda solution, with water, poured into the first ether solution, and the entire ether solution dried with anhydrous magnesium sulfate. The liquid remaining, after distilling off the ether on a water bath, was distilled in vacuo; fractions obtained (at 6 mm); I 94-114°, 2.0 g; II 114-118°, 9.3 g; residue in the flask (tar) 1.5 g.

Fraction II was redistilled, at which time the main mass boiled at 108-109° (4 mm).

Analysis of the Fraction with b.p. 108-109° (4 mm) d_4^{20} 0.9721; n_D^{20} 1.4405; MR_D 66.33. Calculated 65.55.

0.0849 g substance: 0.2013 g CO_2; 0.0788 g H_2O. 0.3346 g substance: 14.10 g benzene: Δt 0.510°. 0.1307 g substance: 14.10 g benzene: Δt 0.198°. Found %: C 64.66; H 10.39; M 241.0, 242.3. $C_{13}H_{24}O_4$. Calculated %: C 63.90; H 9.90. M 244.3.

Upon pouring together semicarbazide acetate and the fraction boiling at 108-109° (4 mm) there was no precipitation. A determination of the percentage active hydrogen (according to Terentev-Shcherbakova) gave a negative result. The substance did not decolorize bromine water or aqueous potassium permanganate.

Saponification of the Dimethylester of Dimethylisobutylglutaric Acid. 25 g of ester, boiling at 136-138° (16 mm), was dissolved in 100 ml of ethyl alcohol (96%), containing 15 g of KOH. The mixture was boiled for 5 hours with a reflux. Upon completion of the heating, the mixture was diluted with 3 times the quantity of

water, and the alcohol evaporated off. A calculated quantity of sulfuric acid was added to the remaining aqueous solution of the potassium salt of the acid. The precipitated solid acid (16.3 g) was recrystallized first from water (granules with m.p. 116-118°), and then from water-acetone mixture from which the acid was obtained in the form of glittering scales with m.p. 124-125°.

0.1195 g substance: 0.2676 g CO_2; 0.1068 g H_2O. 0.1163 g substance: 0.2586 g CO_2; 0.0952 g H_2O. 0.1465 g substance: 18.2 ml NaOH. 0.1556 g substance: 19.3 ml NaOH (T = 0.002982). 0.2489 g substance: 18.92 g acetic acid: Δt 0.312°. Found %: C 61.10, 60.69; H 9.43, 9.16; equiv. 108.0, 108.1; M 210.1. $C_{11}H_{20}O_4$. Calculated %: C 61.08; H 9.26; equiv. 108.15; M 216.3.

To a solution of the sodium salt of the acid, obtained after determination of the neutralization equivalent, there was added the calculated quantity of silver nitrate. The white precipitate of the silver salt was filtered off, washed with water, alcohol, ether, and dried in a vacuum dessicator over sulfuric acid.

0.2000 g substance: 0.1002 g Ag. 0.3027 g substance: 0.1515 g Ag. Found %: Ag 50.10, 50.05. $C_{11}H_{18}O_4Ag_2$. Calculated %: Ag 50.11.

The analytical data corresponded to a,a'-dimethyl-a-isobutylglutaric acid.

Derivation of the Anhydride of a,a'-Dimethyl-a-isobutylglutaric Acid. 11 g of the acid was placed in a Wurtz flask of 200 ml capacity and the acid slowly heated. After 2 hours the temperature had risen to 250°, at which time there distilled off a small volume of water. All of the liquid was then redistilled at 287-300°. The liquid solidified in the condenser. The solid mass was pressed out on a porous plate, and melted at about 60°. 6.7 g of the solid product was obtained, once more distilled, at which time a fraction was obtained boiling at 287-289°. The product was recrystallized several times from petroleum ether (45-75°), shiny needles with m.p. 73-74° were obtained.

0.1089 g substance; 0.2653 g CO_2; 0.0891 g H_2O. 0.1127 g substance: 0.2753 g CO_2; 0.0922 g H_2O. 0.2872 g substance; 14.23 g benzene: Δt 0.522°. 0.2692 g substance: 16.53 g benzene: Δt 0.415°. Found %: C 66.43; 66.64; H 9.16, 9.16; M 200.3, 203.2. $C_{11}H_{18}O_3$. Calculated %: C 66.65; H 9.15; M 198.2.

Transformation of the Anhydride into the Acid and the Silver Salt. 1.0 g of the anhydride, with m.p. 73-74°, was heated in 50 ml of water with 3 g of KOH until all of the oily drops had disappeared from the surface of the liquid. The cooled solution was divided into two equal parts. To one half was added the calculated quantity of sulfuric acid; whereupon $\sim$ 0.35 g of solid substance precipitated, after recrystallization of which from water, and then from acetone-water mixture, melted at 122-123.5°.

A mixed sample with known acid melted at 122-123.5°.

The second half of the alkaline solution was neutralized with dilute nitric acid and to the solution was added the calculated quantity of silver nitrate. The precipitated silver salt of the acid was filtered off from the solution, washed with water, alcohol, ether, and dried in a vacuum dessicator over sulfuric acid.

0.2018 g substance: 0.1012 g Ag. 0.2212 g substance: 0.1108 g Ag. Found %: Ag: 50.14, 50.07. $C_{11}H_{18}O_4Ag_2$. Calculated %: Ag 50.11.

SUMMARY

1. The reaction of the methyl ester of methacrylic acid proceeds "anomalously" with isopropylmagnesium bromide: instead of the expected diisopropylisopropenylcarbinol, there is obtained instead, the dimethyl ester of a,a'-dimethyl-a-isobutyl-glutaric acid, which can only occur by addition of isopropylmagnesium bromide to methyl methacrylate in the 1,4 position. The dimethyl ester of a,a'-dimethyl-a-isobutyl-glutaric acid converts into a,a'-isobutylglutaric acid upon saponification.

2. Upon slow distillation of a,a'-dimethyl-a-isobutylglutaric acid, its anhydride is formed, which readily reconverts back into the salt of the acid upon heating with alkali.

LITERATURE CITED

[1] A. E. Favorsky and A.I. Lebedeva, Collection of Selected Works of Academician A.E. Favorsky, 507 (1940); J. Gen. Chem. 8, 879 (1938). [2] K.A. Ogloblin, J. Gen. Chem. 18, 2153 (1948). [3] A.D. Petrov and Kh. N. Radshabova, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci. 1950, 506; D.G. Young and A.N. Roberts, J. Am. Chem. Soc. 66, 1444 (1944). [4] A. Vogel, J. Chem. Soc. 1933, 1028. [5] E. Kohler, Am. Chem. J., 31, 642 (1904). [6] A. D. Petrov and P.S. Bataev, J. Gen. Chem. 20, 2236 (1950). •

• See Consultants Bureau translation page 2323
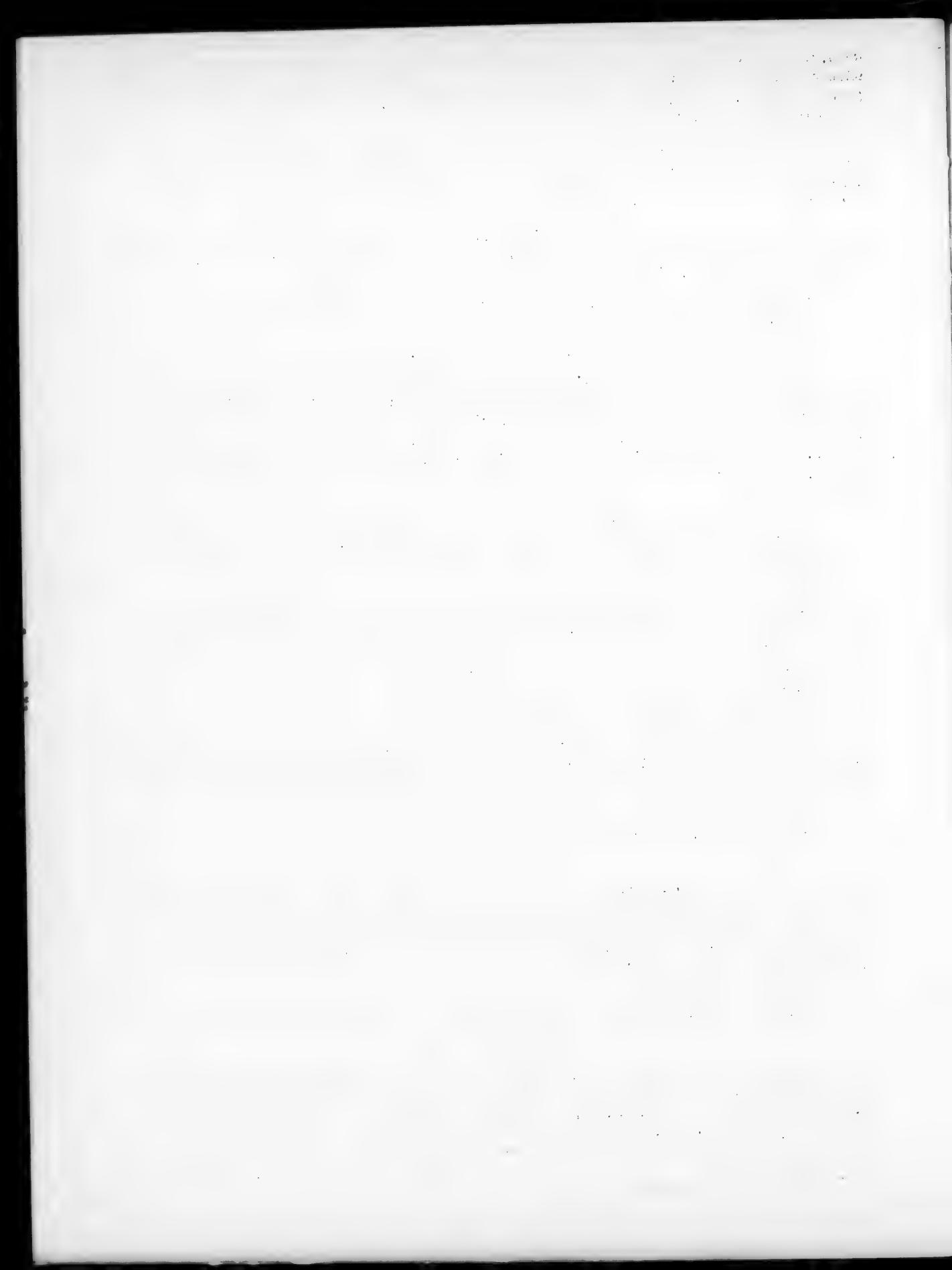
SYNTHESES EMPLOYING ACRYLONITRILE

XVI. THE MECHANISM OF THE CYANETHYLATION REACTION

A. P. Terentyev, A. N. Kost and S. M. Gurvich

At the present time the cyanethylation reaction is understood to be the interaction of acrylonitrile with compounds containing a mobile hydrogen atom. By this method, it is possible, under mild conditions, and in good yields, to introduce one or more β-cyanethyl groups into compounds of different types. The breadth of application of this reaction and it great synthetic possibilities have attracted the attention of many synthesis chemists. In a majority of the cases the cyanethylation reaction requires the use of catalysts. Only the hydrogen halides, ammonia, aliphatic amines and strong bases such as hydrazine or piperidine add to acrylonitrile with heat evolution and without the use of a catalyst. For the most part, the use of alkaline reagents is required. In the presence of strong alkali, water, alcohols, phenols, mercaptans, amides, imides, aldehydes, ketones, nitro compounds, certain hydrocarbons, esters, and other compounds cyanethylate. Aromatic amines do not enter into reaction under normal conditions. For cyanethylation of these compounds, prolonged heating, with the addition of acid, must be employed. All of these reaction conditions were experimentally determined.

The authors assume that addition of acryonitrile occurs in many cases by two different schemes [1].

The acrylonitrile molecule possesses a considerable dipole moment ($\epsilon = 3.88$) due to the presence of the nitrile group, i.e., the molecule has a certain tendency to a negative charge on the nitrogen atom, and on the other side, a tendency to a positive charge on the methylene group:

$$(+) CH_2 = CH - C \equiv N (-).$$

Upon entering into reaction with a substance containing a mobile hydrogen atom, the acrylonitrile evidently forms, at first, an unstable compound at the expense of the methylene group. For realization of such an addition, two situations are theoretically possible: first, linkage to the negatively-charged radical, and secondly — linkage to that atom having a free pair of electrons.

Let us examine the first scheme. In the simplest case, for example in the hydrogen halides, the bond between the hydrogen and the halogen is sharply polarized, the halogen atom being charged negatively, and formation of intermediate compounds occurs easily. Subsequently, there occurs regrouping to the stable state, with the formation of β-haloidopropionitrile:

$$H-Hal + CH_2 = CH - C \equiv N \rightarrow [H-Hal \cdot CH_2 = CH-CN] \rightarrow Hal-CH_2CH_2CN.$$

In hydrogen sulfide, the polarization of the bond is considerably weaker, and therefore it reacts more slowly with the acrylonitrile; upon addition of alkaline agents, however, which polarizes the bond, reaction occurs easily. Alkylmercaptans, for the same reasons react with acrylonitrile only in the presence of alkaline agents, but the arylmercaptans (thiophenols) react comparatively readily without catalysts, where the electron pair placed between the hydrogen and the sulfur atoms is displaced toward the sulfur atom at the expense of the ring influence.

In water and alcohols, polarization of the bond between oxygen and hydrogen atoms is weakly manifested, and therefore reaction occurs only in the presence of alkaline agents. The same phenomenon is observed in compounds capable of cyanethylation with the methylene or methine group. For example, with malonic ester the influence of two carbethoxyl groups imparts a certain tendency to a positive charge on the central carbon atom, but the effect of this charge occurs only under the influence of strong alkaline reagents.

Cyanethylation of compounds containing the amino or imino group is a most interesting case. In

primary aliphatic amines (similarly with hydrazine, hydroxylamine or cyclic derivatives of pyrrolidine or piperidine-type) the ability of the hydrogen atom to ionize is not manifested, but the ability for addition is intensely manifested. Here is observed the second scheme of reaction course, namely, addition of acrylonitrile to a free pair of electrons of the nitrogen atom:

$$
\begin{array}{ccc}
\text{H} & \text{(+)} & \text{(-)} \\
\text{R-N} : & + CH_2{=}CH{-}C{\equiv}N & \rightarrow
\end{array}
\quad
\left[
\begin{array}{c}
\text{H} \\
\text{R-N} : CH_2{=}CH{-}CN \\
\text{H}
\end{array}
\right]
\rightarrow R{-}NH{-}CH_2CH_2CN
$$
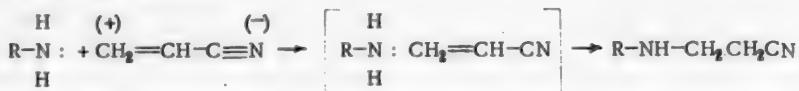
Reaction proceeds vigorously with heat evolution. The yields of N-substituted β-aminopropionitriles are high. We have systematically studied [2] this type of cyanethylation reaction.

Obviously, the greater the basicity of the amine, the easier should be the course of cyanethylation reaction. Observations of this kind were experimentally carried out [3].

The free pair of electrons of the nitrogen atom is drawn toward the carbon-oxygen double bond, or the carbon-carbon bond in amides, imides, pyrrole and indole. The ability for complex formation is weakened and the nitrogen atom acquires the tendency to a positive charge, and the cyanethylation reaction proceeds only in the presence of alkaline agents, i.e., according to the first scheme.

In aromatic amines, the complex-forming properties of the nitrogen atom are considerably weaker than in the aliphatic and the tendency to hydrogen atom ionization is very negligible. Attempts to carry out the reaction according to the first type, i.e. in the presence of alkaline reagents, were unsuccessful; however, it was empirically found that aromatic amines may be cyanethylated in the presence of acid agents (sulfuric, acetic, phosphoric, hydrochloric acids, acetic anhydride) or copper and nickel salts [4].

These catalysts easily form complex compounds with aromatic amines. Upon heating such a complex (where the nitrogen atom is positively charged) there occurs replacement of the anion by the cyanethyl group, with the establishment of a covalent bond and the displacement of the hydrogen atom. Thus, with the aid of external complexing agents, it is possible to direct the reaction according to the second scheme.

Evidently the cyanethylation in the ring of aromatic compounds that takes place in the presence of anhydrous aluminum chloride, even though slowly, can be regarded in the same light.

Thus, the schemes proposed by the authors practically unify all cases of simple cyanethylation and permit a deliberate choice of reaction conditions.

In both schemes we have assumed that the proton displacement occurs in the second stage of the reaction. The case of initial linkage of the proton, we did not examine, because it is known that in the presence of excess protons their slow addition occurs, not to the methine group, but to the nitrogen atom in the acrylonitrile molecule. Thus, for example, upon sulfuric acid reaction, saponification to acrylic acid occurs [6]. Bruson indicated that cyanethylation of carboxylic acids is not possible [6]. It may be that in this case that reaction of the nitrile group with the protons inhibits cyanethylation. Also omitted is the case of addition of acrylonitrile to free neutral radicals, because this case yields mainly polymerization processes, which is quite amply covered in the contemporary literature.

From a cursory inspection of the cyanethylation reaction, it can be seen that in the most interesting instances it occurs under the influence of alkaline reagents and in the American literature so-called "Triton-B" is frequently mentioned, i.e. a 40% solution (aqueous) of trimethylbenzylammonium hydroxide [6].
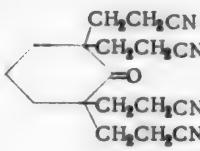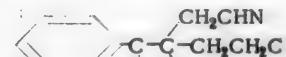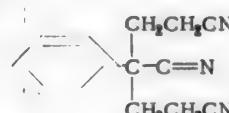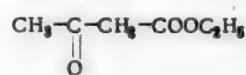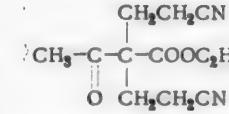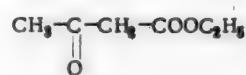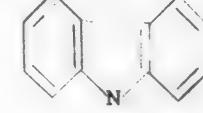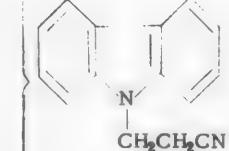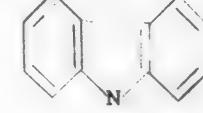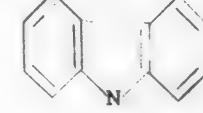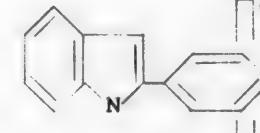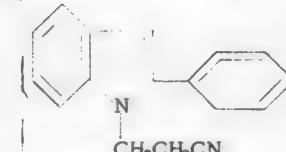
The application of organic bases is explained by their good solubility in organic compounds, as a result of which the reaction goes in homogeneous medium, which of course speeds up the process. Wide-spread advertising by American scientists of the catalyst, "Triton B" is partly connected with these advantages of organic bases, but to a greater degree, it seems, is determined by the interests of the firm which manufactures this catalyst.

V. M. Rodionov and N. G. Yartseva [7] have shown, in the example of phthalimide cyanethylation, that other quaternary ammonium bases can be utilized with equal success, at which time they proposed a simpler and more easily derived agent, namely an alcoholic solution of ethoxytrimethylphenylammonium hydroxide. According to the work of Rodionov and Yartseva there appeared reports by other authors who utilized methyltriethylammonium hydroxide [8] and butoxytrimethylbenzylammonium hydroxide [9] in the capacity of catalysts.

We have run a series of experiments, applying Rodionov's catalyst for the cyanethylation of various compounds, wherein it was found that the cyanethylation reaction proceeds very vigorously in the presence of this catalyst, and the cyanethylation product yields are not worse, and in a series of cases are better than with the use of "Triton B" [1].

The comparative results are quoted in Table 1.

TABLE 1
Cyanethylation in the presence of Rodionov catalyst

Initial substance	Catalyst	Solvent	Temp.	Reaction product	M. pt.	Yield(in%)	Lit.ref.
(cyclohexanone) =O	CR	Benzene	25-50	CH₂CH₂CN / CH₂CH₂CN / =O / CH₂CH₂CN / CH₂CH₂CN	175.5°	95-97	[1]
	TB	"	30-45	"	175	97	[6]
(acetophenone) —C-CH₃ / ‖ O	CR	Benzene	20	C-C-CH₂CH₂CN with CH₂CHN, CH₂CH₂CN ‖ O	129-129.5	65	[1]
	TB	Dioxane	30-40		128-129	57	[6]
	BTBA	ter-C₄H₉OH	20		128-129	64	[9]
(benzyl cyanide) —CH₂—C≡N	Cr	Benzene	25-30	CH₂CH₂CN / C-C≡N / CH₂CH₂CN	71.5	90	[1]
	KOH in CH₃OH	ter-C₄H₉OH	10-25		70	94	[6]
CH₃-C-CH₂-COOC₂H₅ ‖ O	Cr	Benzene	20	CH₂CH₂CN / CH₃-C-C-COOC₂H₅ ‖ O CH₂CH₂CN	82	83	[1]
	TB	Dioxane	20		82	79	[9]
	BTBA	Dioxane	20		82	80	[9]
(diphenylamine) N H	CR	Benzene	0	N CH₂CH₂CN	156.5	89	[1]
	TB	Dioxane	0		155.5	84.5	[10]
(2-phenylindole) N H	CR	Benzene	60	N CH₂CH₂CN	88-89	82	[1]
	TB	Dioxane	60		88.5-89	80	[11]

Conventional symbols: CR - Rodionov catalyst (alcoholic solution of ethoxytrimethylphenylammonia); TB - "Triton B" (40% aqueous solution of trimethylbenzylammonium hydroxide); BTBA - butoxytrimethylbenzylammonia.

It should be noted, however, that the use of quaternary ammonium bases are not always advantageous.

In the presence of alkali or alcoholate the reaction proceeds more slowly but is easier to control. It is also inconvenient to use quaternary ammonium bases in those cases where reaction requires heating to more than 60°, because at this temperature decomposition of the catalyst starts.

In examining the reaction mechanics it is necessary to consider the fact that the cyanethylation process occurs reversibly:

$$R-H + CH_2=CH-CN \rightleftarrows R-CH_2CH_2CN.$$

There are directions in the literature to the effect that cyclohexylamine reacts vigorously with acrylonitrile, forming β-cyclohexylaminopropionitrile, but this compound upon distilling (even in vacuo) breaks down very easily into the initial components [12]. Analogous phenomena were observed upon cyanethylation of certain other amines [10,13]. The presence of an equilibrium system in the cyanethylation of amines is also confirmed by the fact that the yields of cyanethylation products increase if either acrylonitrile or amine is taken in excess [2, 10].

There are fragmentary directions on the reversibility of the reaction in the case of cyanethylation of alcohols and phenols [5, 14]. An assumption has been expressed concerning the reversibility of the reaction between chloroform and acrylonitrile [15]. In one of the preceding articles [16] we demonstrated that upon cyanethylation of ammonia there is set up a dynamic equilibrium in all stages of the reaction.

Thus it may be assumed with sufficient grounds, that all cyanethylation reactions are in equilibrium, to a more or less degree. From this assumption it follows that the introduction into the equilibrium system of another compound, capable of being cyanethylated, can result in additional cyanethylation products:

$$R-CH_2CH_2CN \underset{+RH}{\overset{-RH}{\rightleftarrows}} CH_2=CH-CN \underset{-R'H}{\overset{+R'H}{\rightleftarrows}} R'-CH_2CH_2CN.$$
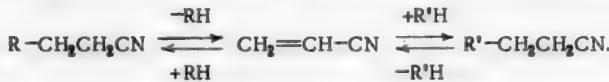
Actually, upon heating β-dimethylaminopropionitrile with piperidine we have observed separation of dimethylamine with formation of β-piperidylpropionitrile:

$$\bigcirc NH + (CH_3)_2N-CH_2CH_2CN \rightarrow (CH_3)_2NH\uparrow + \bigcirc N-CH_2CH_2CN.$$
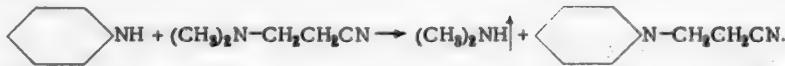
Analogously, there was obtained β-dibutylaminopropionitrile from dibutylamine and the same aminonitrile, during which, as would be expected, the yield of β,N-piperidylpropionitrile was found to be higher, than that of β-dibutylaminopropionitrile as a result of the greater basicity of piperidine.

We indicated earlier [17] that upon heating piperidine with ethylenecyanhydrin, there is formed the piperidine cyanethylation product

$$\bigcirc NH + HO-CH_2CH_2CN \rightarrow \bigcirc N-CH_2CH_2CN.$$

It was found that the same compound is formed upon heating piperidine with β-methoxypropionitrile.

If, instead of piperidine, one takes dibutylamine, then β-dibutylaminopropionitrile is obtained:

$$(C_4H_9)_2NH + CH_3O-CH_2CH_2CN \rightarrow (C_4H_9)_2N-CH_2CH_2CN.$$

The authors have carried out all of the reactions described above without catalysts, because in the reaction medium amine was present.

For carrying out the analogous reaction with malonic ester, the introduction of alkaline catalyst was found to be indispensable. And, namely, β-ethoxypropionitrile does not react under ordinary conditions with malonic ester, but in the presence of sodium ethylate the reaction goes with the formation of mono-ana of di-cyanethylation products of malonic ester.

$$\begin{array}{c} COOC_2H_5 \\ | \\ CH_2 \\ | \\ COOC_2H_5 \end{array} + C_2H_5O-CH_2CH_2CN \xrightarrow{C_2H_5ONa} \begin{array}{c} COOC_2H_5 \\ | \\ CH-CH_2CH_2CN \\ | \\ COOC_2H_5 \end{array}$$

$$\begin{array}{c} \text{COOC}_2\text{H}_5 \\ | \\ \text{CH-CH}_2\text{CH}_2\text{CN} + \text{C}_2\text{H}_5\text{O-CH}_2\text{CH}_2\text{CN} \xrightarrow{\text{C}_2\text{H}_5\text{ONa}} \\ | \\ \text{COOC}_2\text{H}_5 \end{array} \quad \begin{array}{c} \text{COOC}_2\text{H}_5 \\ | \quad \text{CH}_2\text{CH}_2\text{CN} \\ \text{C} \\ | \quad \text{CH}_2\text{CH}_2\text{CN} \\ \text{COOC}_2\text{H}_5 \end{array}$$
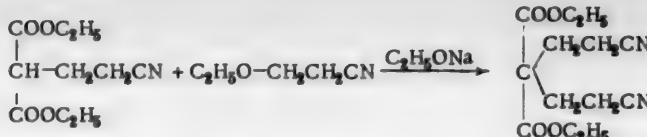
Thus, it appeared that the recyanethylation reaction goes slowly and with evolution of considerable heat, at which time splitting of the O—C bond occurs more easily than the N—C bond.

In the literature there are brief directions [5], on the observation that upon heating the product of dicyanethylation of acetamide with acetamide, in the presence of alkaline agents, there occurs recyanethylation:

$$\text{CH}_3\text{CON(CH}_2\text{CH}_2\text{CN)}_2 + \text{CH}_3\text{CONH}_2 \rightarrow 2\text{CH}_3\text{CONHCH}_2\text{CH}_2\text{CN}$$

It was of interest to attempt to obtain by this method of monocyanethylated compounds of type $\text{R}_2\text{CH-CH}_2\text{CH}_2\text{CN}$ where the cyanethyl group is linked with the carbon atom. As an example acetone was taken, which forms, easily, the tricyanethylated derivative:

$$\text{CH}_3\text{COCH}_3 \xrightarrow{\text{CH}_2=\text{CH-CN}} \text{CH}_3\text{COC(CH}_2\text{CH}_2\text{CN)}_3.$$

Upon heating tricyanethylated acetone with acetone, we presumed to obtain γ-acetobutyronitrile. However, upon combined heating of these substances in the presence of caustic potash for 13 hours at 100° (in a sealed ampoule), or during 6 hours at 150° (in an iron autoclave) we obtained the initial substances and negligible quantity of resin. An attempt to carry out recyanethylation by heating to 100-200° of tri-(β-cyanethyl)-acetone with sodium methylate, or diethylamine, also gave negative results; i.e., it was found that in tricyanethylated acetone, the cyanethyl groups are bound firmly, and under these conditions do not split off.

The results of the authors' experiments on recyanethylation are quoted in Table 2.

EXPERIMENTAL

I. Cyanethylation with Rodionov Catalyst

Rodionov catalyst was prepared according to the method of V. M. Rodionov and N. G. Yartseva [7]. At the time it was noticed that the initial methyl ester of p-tolylsulfoacid should not contain sulfochloride impurity, because otherwise the Rodionov salt turns blue in color, and the activity of the catalyst decreases.

Upon cyanethylation of cyclopentanone and phenylacetonitrile, we examined the influence of sequence of introduction of components into the course of the reaction. If Rodionov catalyst is added to a mixture of acrylonitrile and phenylacetonitrile, then, at low temperatures (0 to 5°) reaction practically fails to go, but if the temperature is raised to 10-15°, a vigorous reaction develops unexpectedly, which acquires the nature of an explosion, even upon adding considerable quantity of neutral solvent (10-15 volumes). The catalyst should therefore be added first and the acrylonitrile then added dropwise.

All compounds obtained by the authors through cyanethylation in the presence of this catalyst (see Table 2) were synthesized by approximately the same methods, and therefore we give a description of a typical experiment.

Cyanethylation of Cyclopentanone. S. V. Vitt participated in the carrying out of the experiment. 21 g (0.25 mole) of cyclopentanone, 250 ml of dry benzene and 1 ml of freshly prepared Rodionov catalyst were placed in a flask equipped with stirrer, reflux condenser, thermometer and dropping funnel. With vigorous stirring and external water-cooling, 58 g (1.1 mole) of acrylonitrile was introduced dropwise over a period of 3 hours, the temperature being maintained at 25-30°. If precipitation of crystals was not observed after the addition of 5-8 ml of acrylonitrile, then further addition was stopped, the mixture carefully heated by warm water (not higher than 40°) and 5-6 drops of catalyst added if necessary. After completion of the acrylonitrile addition, the solidified mass was mixed for 2 hours at 40-50°, and left for the night at room temperature. The crystals were then cooled and filtered off by suction. 71-72 g (i.e., 95-97 % of theoretical) of 2,2,5,5-tetra-(β-cyanethyl)-cyclopentanone with m.p. 175.5° was obtained.

Literature data: m.p. 175° (from methylethylketone) [6].

II. Recyanethylation Reactions

1,1,1-Tri-(β-cyanethyl)-acetone was obtained in yield of 73% by reaction of acrylonitrile at 45° with excess acetone in the presence of sodium ethylate. M.p. 151, which corresponds to the literature data [18]. β-Dimethylaminopropionitrile was obtained by a modified method of A.P. Terentyev and A.N Kost [19]. 53 g (1 mole) of acrylonitrile was added in small portions, with vigorous stirring, to 120 g of 50% aqueous solution (1.33 mole) of dimethylamine, after which the mixture was heated under reflux for 5 hours on a water bath. The reaction product was salted out by addition of 50 g of potash, was separated, dried with fused potash, and distilled. 71.5 g of β-dimethylaminopropionitrile was obtained: b.p. 169-171° at 745 mm. Yield 73% of theory.

TABLE 2
Recyanethylation reaction

Cyanethylated compound	Cyanethylating agent	Catalyst	Reaction conditions		Compound obtained	Yield (in %)
			Time(hrs)	Temp.		
(piperidine ring)NH	$(CH_3)_2N-CH_2CH_2CN$		10	160°	(piperidine ring)$N-CH_2CH_2CN$	30
$(C_4H_9)_2NH$		Without catalyst	40	170	$(C_4H_9)_2N-CH_2CH_2CN$	20
(piperidine ring)NH	$CH_3O-CH_2CH_2CN$		15	120	(piperidine ring)$N-CH_2CH_2CN$	13
$(C_4H_9)_2NH$			16	180	$(C_4H_9)_2N-CH_2CH_2CN$	15
$COOC_2H_5$ CH_2 $COOC_2H_5$	$C_2H_5O-CH_2CH_2CN$	C_2H_5ONa	10	100	$(C_2H_5OOC)_2CH-CH_2CH_2CN$ $(C_2H_5OOC)_2C(CH_2CH_2CN)_2$	27 10
$CH_3-\overset{O}{\overset{\|}{C}}-CH_3$	$CH_3-\overset{O}{\overset{\|}{C}}-C(CH_2CH_2CN)_3$	KOH	13	100	Recyanethylation products not found	
$CH_3-\overset{O}{\overset{\|}{C}}-CH_3$		KOH	6	150		
$(C_2H_5)_2NH$		Without catalyst	7	60		
CH_3OH		CH_3ONa	7	60		
CH_3OH		KOH	2	200		

β-Methoxy- and β-ethoxypropionitrile were obtained by cyanethylation of the corresponding alcohols in the presence of sodium alcoholate [14].

Cyanethylation of β-dimethylaminopropionitrile. a) A mixture of 9.8 g (0.1 mole) of β-dimethylamino-propionitrile and 15 g (0.17 mole) of piperidine was heated for 10 hours at 160°, during which time continuous evolution of dimethylamine was observed. The piperidine excess was then distilled off, and the residue fractionally distilled in vacuo. Two fractions were obtained: 1st fraction – 6.7 g; b.p. 45-47° at 4 mm; n_D^{20} 1.4920; represented the initial β-dimethylaminopropionitrile. 2nd fraction – 4.1 g; b.p. 77-78° at 3 mm; n_D^{20} 1.4702; d_4^{20} 0.9438; from the constants was identified as β,N-piperidylpropionitrile. The picrate, m.p. 158° (from alcohol) did not give depression with the picrate of β,N-piperidylpropionitrile. Yield of β,N-piperidylpropionitrile was 30% of theory, on the basis of β-dimethylaminopropionitrile.

b) A mixture of 14.7 g (0.15 mole) of β-dimethylaminopropionitrile and 12.9 g (0.1 mole) of dibutyl-amine was heated for 40 hours at 170° (to the cessation of dimethylamine evolution). After cooling, the reaction mixture was fractionally distilled in vacuo. After distillation of the reaction mixture there was obtained 3.7 g of fraction, b.p. 112-113° at 7 mm; identified as β-dibutylaminopropionitrile; yield 20% of theory; n_D^{20} 1.4450; d_4^{20} 0.8604; MR_D 56.39. $C_{11}H_{22}N_2$. Calculated MR_D 56.76. Picrate m.p. 76° (from alcohol), which corresponded to the literature value [3, 10].

Cyanethylation of β-alkoxypropionitrileamine. a) A mixture of 8.5 g (0.1 mole) of β-methoxypropion-itrile and 8.5 g (0.1 mole) of piperidine was heated for 15 hours at 120°. After cooling, the mixture was distilled in vacuo. 1.8 g (13% of theory) β-N-piperidylpropionitrile was obtained. B.p. 76-77° at 3 mm; n_D^{20} 1.4680; d_4^{20} 0.9463. Picrate, m.p. 157° (from alcohol).

b) A mixture of 8.5 g (0.1 mole) of β-methoxypropionitrile and 12.9 g (0.1 mole) of dibutylamine was heated for 16 hours at 180°, and afterwards distilled in vacuo. 2.8 g of β-dibutylaminopropionitrile, i.e. 15% of theory, was obtained. B.p. 98-100° at 3 mm; n_D^{20} 1.4448; d_4^{20} 0.8581. Picrate, m.p. 76° (from alcohol).

c) To a solution of sodium ethylate (2.3 g of sodium in 40 ml of absolute ethyl alcohol) was added 32 g

(0.2 mole) of malonic ester and 9.9 g (0.1 mole) of β-ethoxypropionitrile. The mixture was heated for 10 hours on a water bath, and then 3 times the volume of water was added, acidified with hydrochloric acid, and extracted 4 times with ether. The ether extract was dried with anhydrous sodium sulfate, the ether distilled off, and the residue distilled in vacuo. The products of mono- and di-cyanethylation of malonic ester were obtained. The monocyanethylation product (ethyl ester of α-carbethoxy-γ-cyanbutyric acid) was obtained in quantity amounting to 5.7 g (i.e. 27% of theory). B.p. 140-142° at 5 mm; n_D^{20} 1.4380; d_4^{20} 1.0881; MR_D 51.44; $C_{10}H_{15}O_4N$. Calculated MR_D 51.51. The dicyanethylation product (the dinitrile of γ,γ-dicarbethoxypimelic acid) was obtained in an amount equal to 1.3 g (i.e., 10% of theory). B.p. 193-198° at 5 mm; m.p. 61° (from alcohol).

The constants for both substances corresponded to the literature data [20].

Cyanethylation with tri-(β-cyanethyl)-acetone. a) A mixture of 4.3 g of tri-(β-cyanethyl)-acetone, 18 ml of dry acetone and 0.5 g of solid caustic potash was heated for 13 hours in a sealed flask at 100°. The brown mixture was diluted with double the volume of water and extracted with ether. Upon distillation of the dried ether extract in vacuo, it was not possible to separate the nitrile of γ-acetobutyric acid. The residue after recrystallization from alcohol was found to be the initial tri-(β-cyanethyl)-acetone with m.p. 151°.

An analogous result was obtained upon heating 3 g of tri-(β-cyanethyl)-acetone and 10 ml of acetone in an iron tube for 6 hours at 150° (in the presence of 0.1 g of caustic potash).

b) 0.5 g of sodium was dissolved in 25 ml of absolute methyl alcohol, and then 3 g of tri-(β-cyanethyl)-acetone was added, and the mixture heated for 7 hours under reflux. After cooling, the mixture was neutralized with acetic acid and dried. After distillation of the methyl alcohol and acetone (in vacuo), there remained only the initial tri-(β-cyanethyl)-acetone.

In a second experiment, the vapors of methyl alcohol were conducted through liquid tri-(cyanethyl)-acetone in the presence of caustic potash at 200° for 2 hours. The distillate contained only methyl alcohol. From the reaction flask, in vacuo, up to 200°, nothing distilled over. The residue resinified partially, tri-(β-cyanethyl)-acetone.

c) A mixture of 3 g of tri-(β-cyanethyl)-acetone and 20 ml of diethylamine was heated for 7 hours under reflux. Then the amine was distilled off in vacuo, but the residue was found to be only the initial tri-(cyanethyl)-acetone.

SUMMARY

1. A mechanism was proposed for the cyanethylation reaction, which gives the possibility for explaining and choosing beforehand the catalysts for this reaction.

2. The wide application of ethoxytrimethylbenzylammonium hydroxide (Rodionov catalyst) in the capacity of an alkaline agent for cyanethylation reactions was demonstrated.

3. The reversibility of the cyanethylation reaction was proven in a series of examples. Several cases of recyanethylation were investigated.

LITERATURE CITED

[1] A. P. Terentyev and A. N. Kost, Reports of the Scientific works of the Members of the D.I. Mendeleev All-Union Chem. Soc. 1950, No. 4, 1; News of the Moscow State University, 1950, No. 12, 71. [2] A.P. Terentyev J. Gen. Chem. 12, 415 (1942); A.P. Terentyev, and A.N. Kost, J. Gen. Chem. 16, 859 (1946); 20, 1275 (1950); A.N. Kost, News of the Moscow State Univ. 1947, No. 2, 141; Scientific Notes, Moscow State Univ. VI, No. 131, 37 (1950). [3] J. Burckhalter, E. Jones, W. Holcomb, L. Sweet, J. Am. Chem. Soc. 65, 2014 (1943). [4] A.P. Terentyev and A.N. Kost and V.M. Potapov, J. Gen. Chem. 18, 82 (1948); A.F. Bekhli; and A.G. Serebrenikova, J. Gen. Chem. 19, 1553 (1949). [5] O. Bayer, Z. Ang. Chem., 61, 229 (1949). [6] H. Bruson, Org. React. V, N.Y., 1949. [7] V.M. Rodionov and N.G. Yartseva, Bull. Acad. Sci. U.S.S.R., 1948, 251. [8] G. Buckley, T. Elliott, F. Hunt, A. Lowe, J. Chem. Soc., 1947, 1505. [9] G. Zellars, R. Levine, J. Org. Chem., 13, 911 (1948). [10] F. Whitmore, H. Mosher, R. Adams, R. Taylor, E. Chapin, C. Weisel, W. Janko, J. Am. Chem. Soc., 66, 725 (1944). [11] R. Blume, H. Lindwall, J. Org. Chem., 10, 255 (1945). [12] U. Hoffmann, B. Jacobi, German patent 598. 185 (1931); Frdl., 20, I, 346; D. Tarbell, W. Shakespeare, C. Claus, J. Bunnett, J. Am. Chem. Soc., 68, 1217 (1946). [13] G. Bachman, R. Mayhew, J. Org. Chem., 10, 245 (1945). [14] W. Utermohlen, J. Am. Chem. Soc., 67, 1505 (1945). [15] H. Bruson, W. Niederhauser, T. Riener, W. Hester, J. Am. Chem. Soc. 67, 601 (1945). [16] A. P. Terentyev, K. I. Chursina and A.N. Kost, J. Gen. Chem. 20, 1073 (1950). [17] A.P. Terentyev and A. N. Kost, J. Gen. Chem. 18, 510 (1948). [18] H. Bruson, T. Renier, J. Am. Chem. Soc. 64, 2850 (1942); A.P. Terentyev and S.M. Gurvich, News of the Moscow State Univ. 1950, No. 5, 47. [19] A.P. Terentyev and A.N. Kost, J. Gen. Chem. 17, 1632 (1947). [20]. G. Hesse, E. Bucking, Ann, 563, 31 (1949).

Moscow State University, Academician N.D. Zelinsky Laboratory
of Organic Chemistry

* See Consultants Bureau translation page 1563. ** See Consultants Bureau translation page 1115.

PREPARATION OF RICINOLEIC ACID OXIDE

G. V. Pigulevsky and E. M. Rostomyan

The first studies on preparation of oxides of ricinoleic acid and of its isomer-ricinelaidic acid, were reported by Boeseken and his co-workers [1,2]. These authors obtained ricinoleic acid oxide by oxidation of methyl ricinoleate using benzoyl peroxide with subsequent saponification of the oxidation product. Ricinoleic acid oxide, separated from salts, was liquid and had $[a]_D^{14}$ −6.6°. It must be noted that only the initial ricinoleic acid appears to have been sufficiently purified. The subsequent steps — preparation of the methyl ester, its oxidation, and separation of the liquid ricinoleic acid oxide — were not accompanied by any purification; consequently there is insufficient assurance of purity in the prepared oxide.

We set ourselves the task, employing results of our earlier studies [3], of synthesizing ricinoleic acid oxide, passing through stages of preparing the acid by individual steps.

The reaction was carried out according to the following scheme:

$$CH_3-(CH_2)_5-CHOH-CH_2-CH=CH-(CH_2)_7-COOCH_3 \xrightarrow{(CH_3CO)_2O}$$
$$\text{(I)}$$

$$CH_3-(CH_2)_5-CH(OCOCH_3)-CH_2-CH=CH-(CH_2)_7-COOCH_3 \xrightarrow{CH_3COOOH}$$
$$\text{(II)}$$

$$CH_3-(CH_2)_5-CH(OCOCH_3)-CH_2-\overset{O}{\overset{\diagup\diagdown}{CH-CH}}-(CH_2)_7-COOCH_3 \rightarrow$$
$$\text{(III)}$$

$$\xrightarrow{KOH+C_2H_5OH} CH_3-(CH_2)_5-CHOH-CH_2-\overset{O}{\overset{\diagup\diagdown}{CH-CH}}-(CH_2)_7-COOH$$
$$\text{(IV)}$$
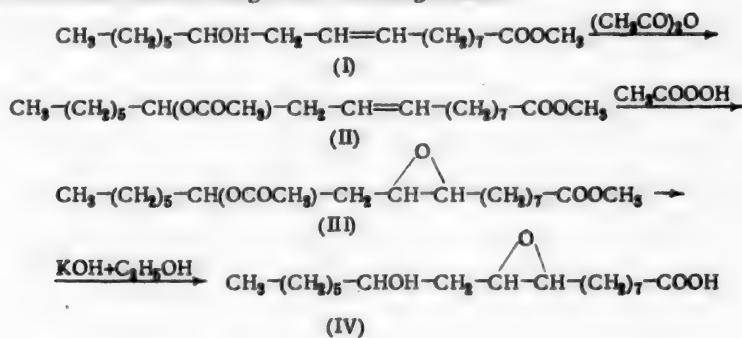
EXPERIMENTAL

Caster oil with an iodine number of 88.3 served as the starting material. The acid separated from caster oil was esterified with methyl alcohol in the presence of HCl (5%). The esterified acid was subjected to fractional distillation under vacuum (0.26 mm). A fraction was separated boiling within the limits of 189-193° with a_D + 5.00°.

According to the literature, b.p. is 245° (10 mm); a_D + 4.68°.

Ricinoleic acid methyl ester (I) was acetylated under usual conditions. The acetylated product was subjected to fractional distillation. The main fraction, boiling between the limits of 181 and 184° (0.14 mm), had the following properties:

d_4^{20} 0.9475; n_D^{20} 1.45697; a_D + 20.08°. Iodine No. 76.08 (calculated 71.75).

0.1251 g substance: 0.3286 g CO_2; 0.1249 g H_2O. 0.1242 g substance: 0.2999 g CO_2; 0.1140 g H_2O. 1.1524 g substance: 0.3499 g KOH. 1.1006 g substance: 0.3375 g KOH. Found %: C 71.63, 71.62; H 11.16, 11.16; saponification number 303.2, 306.6. $C_{21}H_{38}O_4$. Calculated %: C 71.19; H 10.73; saponification number 316.4.

The acetylated ester (III) (a_D + 20.68) was oxidized by acetyl peroxide in presence of ether. Acetyl peroxide was taken in some excess (10%). Oxidation was completed in 10 days. The oxide of acetylated methyl ester of ricinoleic acid was fractionally distilled under vacuum (0.12 mm). A fraction with b.p. 187-188° was separated.

a_D + 10.12°; d_4^{20} 0.9819; n_D^{20} 1.45407; MR_D 102.06; calculated 101.93.

0.1238 g substance: 0.3095 g CO_2; 0.1187 g H_2O. 0.1115 g substance; 0.2792 g CO_2; 0.1065 g H_2O. 0.3610 g substance: 0.1060 g KOH; 0.3416 g substance: 0.1012 g KOH. Found %: C 68.18, 68.29; H 10.73, 10.68; saponification number 293.7, 296.3. $C_{21}H_{38}O_5$. Calculated %: C 68.10; H 10.20; saponification number 303.2.

The analytical results show that we prepared the oxide of acetylated methyl ester of ricinoleic acid (III).

The oxide was saponified cold with alcoholic caustic. By addition of the calculated quantity of sulfuric acid to the potassium salt, ricinoleic acid oxide was separated. The latter was extracted using ethyl ether. On evaporation of the ether, the oxide crystallized. M.p. 30-31°. The oxide (IV) was readily soluble in alcohol and poorly soluble in petroleum ether. $[a]_D^{19} -6.68°$.

0.1120 g substance: 0.2816 g CO_2; 0.1135 g H_2O. 0.1168 g substance: 0.2941 g CO_2; 0.1167 g H_2O. Found %: C 68.57, 68.67; H 11.24, 11.18. $C_{18}H_{34}O_4$. Calculated %: C 68.79; H 10.83.

SUMMARY

1. Acetylated ricinoleic acid methyl ester was prepared; it showed high rotation of the polarization plane, $[a]_D +21.2°$.

2. The oxide of acetylated ricinoleic acid methyl ester, prepared for the first time, had the following properties: $[a]_D^{19} +10.31°$; d_4^{20} 0.9819; n_D^{20} 1.45407.

3. Ricinoleic acid oxide, prepared from the oxide of the acetylated methyl ester, was a solid; m.p. 30-31°, $[a]_D^{19} -6.68°$.

LITERATURE CITED

[1] J. Boeseken, W. Smit, Gaster, Proc. Acad. Sci. Amst. 32, 377 (1929).

[2] W. Smit, Rec. trav. chim., 49, 673 (1930).

[3] G. V. Pigulevsky and L. V. Rokityansky, J. Gen. Chem. 7, 882 (1937).

Laboratory for Natural Compounds
Leningrad State University

PREPARATION OF $\Delta^{2,3}$-HEXADECENOIC ACID

P. A. Artamonov

Unsaturated hexadecenoic acids, with the double bond in various locations, have remained incompletely studied to the present time. Of the acids of this series, the most investigated appears to be fisitolic acid ($\Delta^{9,10}$) first prepared by Hofstadter [1] from sperm oil. Later it was separated from seal oil by Lyubarsky [2] and by Bauer and Neth [3]; Armstrong and Hilditch [4] prepared it from whale blubber and established its structure. The existence of hypogeic acid [5] is rejected in the studies of a series of investigators [6-9]. Zoomaric acid and the so-called "Bull's acid" are reported to be identical to fisitolic acid (9-hexadecene-1-oic acid) by Toyama [10,11, 12]. In consequence of this study, the confusion which has existed to the present time in the literature on the relationships among the acids of this series, has been resolved. The remaining acids of the series, including the synthetically prepared 7-hexadecene-1-oic and 2-hexadecene-1-oic acids appear incompletely studied and their structure not fully established.

A study of unsaturated hexadecenoic acids has considerable theoretical and practical interest: the same number of carbon atoms occurs in palmitic acid which enters the constitution of many vegetable oils and the fat of marine animals and plays a major role in the fat industry for the manufacture of high-grade hydrogenated edible fats, the nature of which remain incompletely worked out up to the present time. Still it has been shown that hydrogenated fats contain considerable quantities of isoacids, even including those of hexadecenoic acids. The mechanism of formation of isoacids during hydrogenation of fats, and also their behaviour with oxygen, hydrogen, and other reagents has hardly been studied up to the present time. Incompletely studied is also the question of the influence of isoacids on structure and food quality of hydrogenated fats. The literature method reported for preparation of isoacids by splitting out of bromine from brominated derivatives of saturated fatty acids has not been studied sufficiently.

EXPERIMENTAL

The first report on $\Delta^{2,3}$-hexadecenoic acid was given by Ponzio [13]; by the action of alcoholic potassium hydroxide on iodopalmitic acid an unsaturated acid with m.p. 49° was obtained; proof of structure or description of properties were not given.

For the synthesis of $\Delta^{2,3}$-hexadecenoic acid we started with chemically pure palmitic acid [purified by repeated fractional crystallization from benzene (65-70° fraction) and ethyl alcohol] having an m.p. of 62.6-63°. Bromination of the acid was by the method of Hell and Sadowsky [14], previously used by us in the synthesis of $\Delta^{2,3}$-octadecenoic acid [15].

500 g finely divided palmitic acid was charged into a flask (approximately 3 liters capacity), and carefully mixed with 40 g red phosphorous; after this 300 g bromine was cautiously added (over a period of 3 hours) from a dropping funnel. After all the bromine was introduced, when intensity of reaction decreased, the flask's contents were heated on a water bath until hydrogen bromide and excess bromine were removed. A solution of sodium bisulfite was then carefully added until color was removed. α-Brompalmitic acid was extracted using petroleum ether ($\sim$ 1:6) after 2-3 washes of the dense oily mass with warm water. The ether extract was filtered through paper; the crystals of α-brompalmitic acid which settled after several hours were subsequently recrystallized from the same solvent.

α-Brompalmitic acid purified by this procedure melted at 53-53.5°, in full agreement with the literature value [16]. The yield was 523 g (84% of theoretical).

Analysis for bromine content (by the Stepanov method) [17]:

0.2150 g substance: 0.1198 g AgBr 0.2200 g substance: 0.1233 g AgBr. Found %: Br 23.71, 23.86. $C_{16}H_{31}O_2Br$. Calculated %: Br 23.85.

α-Brompalmitic acid – crystals of acicular structure and pearly lustre – is readily soluble in organic solvents (petroleum ether, alcohol, acetone, and others).

α-Brompalmitic acid was then treated with an alcoholic solution of potassium hydroxide according to the methods of Ponzio [13] and Le Sueur [18] in order to split out hydrogen bromide and form $\Delta^{2,3}$-hexadecenoic acid. This method was first used by them to prepare $\Delta^{2,3}$-octadecenoic acid from α-bromstearic acid although it was found that the yield of $\Delta^{2,3}$-octadecenoic acid was insignificant. To 100 g α-brompalmitic acid in a porcelain dish was added 240 ml of 30% alcoholic potassium hydroxide (c.p.). The mixture was then heated for 3 hours on a water bath until the alcohol was completely removed. The reaction mass was then diluted with water and made slightly acid with 10% sulfuric acid. The oily material rising to the surface was quickly separated from the liquid and extracted with ethyl ether. The ether extract was dried with calcium chloride, and following separation from the calcium chloride, the ether was evaporated. The residual solid fatty acid, which was a quite brittle mass, was subjected to fractional separation: it was finely crushed in a mortar and dissolved at room temperature in petroleum ether in the ratio of 1:10. The settled material, insoluble in petroleum ether, was separated from the filtrate and set aside (Fraction 1). Petroleum ether in the filtrate was evaporated and the fatty acid residue dissolved in ethyl alcohol in the ratio of 1:5. The alcoholic solution was cooled to minus 5-6°: a small quantity of precipitate (clearly crystalline in structure) formed and was readily removed from the mother liquor by low-temperature filtration (Fraction 2). After the removal of this precipitate, the filtrate was cooled to minus 5-6° again: an additional small quantity of precipitate (crystalline) was obtained and combined with Fraction 2. Following separation of Fraction 2, the filtrate was cooled to minus 10-12°; the copious amorphous precipitate which separated was removed by low-temperature filtration and set aside (Fraction 3). The yields of the fractions are given in the table.

| Run No. | Quantity of | | Fraction 1 | | Fraction 2 | | Fraction 3 | |
	Brompalmitic acid (in grams)	Solid residue after splitting out bromine (in g)	Grams	%	Grams	%	Grams	%
1	100	70.0	16.0	22.85	3.65	5.15	50.4	72
2	100	76.0	18.0	23.68	5.6	7.37	52.4	68.94
3	100	74.5	17.6	23.62	4.9	6.57	52.0	69.80
4	100	74.9	19.0	25.36	3.5	4.68	52.4	69.95
5	100	74.1	16.0	21.58	2.8	3.78	55.3	74.64

Investigation of Fraction 1. The first residue, separated from the products obtained by treating α-brompalmitic acid with alcoholic caustic, after recrystallization from chloroform (lustrous prisms) melted at 88.5-89° and was not soluble in petroleum ether. It was readily soluble in chloroform and in alcohol with heating. It was evidently α-hydroxypalmitic acid, formed by replacement of bromine by a hydroxyl group (according to the literature [19], its m.p. is 86.5-87°).

0.2406 g substance: 0.6167 g CO_2; 0.2613 g H_2O. 0.1609 g substance: 0.4158 g CO_2; 0.1707 g H_2O. 0.3658 g substance: 13.4 ml 0.1 N KOH. 0.4013 g substance: 14.75 ml 0.1 N KOH. 0.7900 g substance: 5.03 ml 0.5 N KOH. 0.8156 g substance: 5.34 ml 0.5 N KOH. Found %: C 69.91, 70.48; H 12.16, 11.88. Acid no. 205.54, 205.81; hydroxyl number by the Normann [20] method, 178.6, 183.6; number of OH groups 1.00, 1.02. $C_{16}H_{32}O_3$. Calculated %: C 70.55; H 11.85. Acid number 206.09; hydroxyl number 178.5.

On the basis of all the above data, we may conclude that the Fraction 1 substance was definitely α-hydroxypalmitic acid.

Investigation of Fraction 2. This fraction separated from the products melted at 49-49.5° and was readily soluble in many organic solvents. It crystallized well from alcohol and petroleum ether in the form of shiny rods and evidently appeared to be an unsaturated hexadecenoic acid.

0.1214 g substance: 0.3390 g CO_2; 0.1281 g H_2O. 0.1517 g substance: 0.4240 g CO_2; 0.1600 g H_2O. 0.3476 g substance: 13.65 ml 0.1 N KOH. 0.3784 g substance: 14.90 ml 0.1 N KOH. Found %: C 76.15, 76.20; H 11.82, 11.81; M 254.65, 254.00. $C_{16}H_{30}O_2$. Calculated %: C 75.52; H 11.89; M 254.24.

The material under consideration had an iodine number, determined by the Hubl method, of 26.3 (theoretical 99.78). It is known from the literature [21] that the closer the double bond is to the carboxylic group, the less

is the iodine number.

In order to determine whether it would be possible to approach the theoretical iodine number, experiments were set up with longer holding times than those recommended (by Hubl); the following results were obtained: 26.3 in 24 hours, 46.7 in seven days, 90.0 in 18 days. Evidently, the theoretical iodine number may be attained in this manner for the material under study.

The substance was subsequently subjected to saturation hydrogenation: palmitic acid with m.p. 63° was obtained.

The above data demonstrated indisputably that the material under study in Fraction 2 was an unsaturated acid. In order to fix the location of the double bond, the acid was subjected to oxidative cleavage. For this, 150 ml of a 10% solution of KOH was added to 3 g of the acid. A 5% solution of potassium permanganate was then added step-wise with stirring. The mixture was heated on a water bath and allowed to stand overnight. On the following day, the mixture was decolorized by a solution of sodium bisulfite in the presence of 10% sulfuric acid. The fatty acid which came to the surface, on decolorization and solution of the MnO_2, was extracted by petroleum ether. After two recrystallizations, this material melted at 53.6°, and evidently was myristic acid.

0.2100 g substance: 0.5643 g CO_2; 0.2387 g H_2O. 0.3560 g substance: 15.60 ml 0.1 N KOH. 0.2670 g substance: 11.66 ml 0.1 N KOH Found %: C 73.28; H 12.78. Acid no. 245.87, 245.03. $C_{14}H_{28}O_2$. Calculated %: C 73.61; H 12.36. Acid no. 245.42.

The analytical results confirm the presence of myristic acid. No depression was observed in a mixed melting point test with myristic acid.

Consequently, the unsaturated acid subjected by us to oxidative cleavage appears to have been $\Delta^{2,3}$-hexadecenoic acid $CH_3(CH_2)_{12}CH{=}CHCOOH$.

The silver salt of $\Delta^{2,3}$-hexadecenoic acid $C_{16}H_{29}O_2Ag$ was prepared by the action of 0.1 N $AgNO_3$ solution on an alcoholic solution of the sodium salt of the acid under study; it was a crystalline powder of grayish color.

0.1820 g substance: 0.3537 CO_2; 0.1302 g H_2O; 0.0546 g Ag. Found %: C 53.0; H 8.0; Ag 30.0. $C_{16}H_{29}O_2Ag$. Calculated %: C 53.16; H 8.09; Ag 29.87.

The lead salt of $\Delta^{2,3}$-hexadecenoic acid $(C_{16}H_{29}O_2)_2Pb$ was prepared by the action of lead acetate on a warm alcoholic solution of the sodium salt of this acid; it was a white crystalline powder with m.p. 141°.

0.1510 g substance: 0.0635 g $PbSO_4$. Found %: Pb 28.70. $(C_{16}H_{29}O_2)_2Pb$. Calculated %: Pb 29.04.

Ethyl ester of $\Delta^{2,3}$-hexadecenoic acid. 2 g $\Delta^{2,3}$-hexadecenoic acid and 20 ml absolute alcohol were placed in a 50 ml flask fitted with an air condenser; 4 ml concentrated sulfuric acid was then added. The mixture was heated on a water bath for 30 minutes. The ester formed was separated, washed until neutral, and recrystallized from methyl alcohol. $\Delta^{2,3}$-hexadecenoic acid ethyl ester melted at 16°; and was readily soluble in alcohol, acetone, and other solvents.

0.2204 g substance: 0.6149 g CO_2; 0.2380 g H_2O. Found %: C 76.08; H 12.09. $C_{16}H_{29}OOC_2H_5$. Calculated %: C 76.52; H 12.14.

Investigation of Fraction 3. This acid fraction was readily soluble in most organic solvents and melted at 36-38°. This substance, evidently, appeared to be α-ethoxypalmitic acid, formed as a result of replacing bromine by an OC_2H_5 group during reaction of alcoholic caustic on α-brompalmitic acid.

0.2100 g substance: 0.5478 g CO_2; 0.2258 g H_2O. 0.3150 g substance: 0.8317 g CO_2: 0.3358 g H_2O. 0.3293 g substance: 10.95 ml 0.1 N KOH 0.3592 g substance: 11.95 ml 0.1 N KOH Found %: C 71.12, 72.00; H 12.03, 11.94. Acid no. 186.6, 186.7. $C_{18}H_{36}O_3$. Calculated %: C 71.93; H 12.08. Acid no. 186.85.

These data demonstrate that Fraction 3 of the product under study was in fact α-ethoxypalmitic acid $CH_3(CH_2)_{13}CHOC_2H_5COOH$.

Thus, the yield of $\Delta^{2,3}$-hexadecenoic acid was very low, falling within the limits 3.78-7.37%.

In the splitting of hydrogen bromide from α-brompalmitic acid by an alcoholic solution of KOH, what mainly occurs is substitution of bromine by the OH group with formation of α-hydroxypalmitic acid (21.58-

25.36%) or by the OC_2H_5 group with formation of the ethylated acid (68.94-74.64%).

SUMMARY

1. $\Delta^{2,3}$-hexadecenoic acid was prepared in the chemically pure form, its structure was proven and its properties studied.

2. The preparation of unsaturated acids via brom-derivatives of saturated fatty acids is not very effective: for the most part the reaction leads to replacement of bromine by an OH-group with formation of α-hydroxypalmitic acid or by an OC_2H_5-group with formation of α-ethoxypalmitic acid.

LITERATURE CITED

[1] P. Y. Hofstadter, Ann. Chem. and Pharm. 91, 177 (1854).

[2] E. L. Lyubarsky, J. Prac. Chem. (2), 57, 19 (1898).

[3] A. Bauer and Neth, Chem. Umschau, 31, 5 (1924).

[4] E. Armstrong and T. Hilditch, J. Soc. Chem. Ind., 44, 180 (1925).

[5] A. Gofsman and Scheven, Ann. Chem. and Pharm., 94, 230 (1855).

[6] T. Hilditch and N. Vidyarthi, J. Soc. Chem. Ind., 46, 172 (1927).

[7] G. S. Jamieson, Baughman and Brauns, J. Am. Chem. Soc., 43, 1372 (1921).

[8] L. Schon, Ann, 244, 253 (1888).

[9] Ph. Kreiling, Ber., 21, 880 (1888).

[10] Y. Toyama, Chem. Umschau, 31, 221 (1924).

[11] Y. Toyama, J. Soc. Chem. Ind., 30, 603 (1927).

[12] H. Bull., Ber., 39, 3570 (1906).

[13] G. Ponzio, Gazz. Chem. Ital., 35, 11, 132 (1905).

[14] C. Hell and Y. Sadowsky, Ber., 24, 2388 (1891).

[15] G. V. Pigulevsky and P. A. Artamonov, J. Gen. Chem. 12, 510 (1942).

[16] C. Hell and Iordanow, Ber., 24, 938 (1891).

[17] D. Torp and M. Uaitli (translator's note — Thorpe and Whiteley ?). Practical Handbook of Organic Analysis, p. 60 (1937).

[18] H. R. LeSueur, J. Chem. Soc., 85, 1708, (1904).

[19] H. R. Le Sueur, J. Chem. Soc., 87, 1895 (1905).

[20] W. Normann, Fettchem. Umschau, 10, 194 (1933).

[21] A. Eckert and O. Haller, Monatsh., 34, 1815 (1913).

[22] A. W. Ralston, Fatty acids and their derivatives (1948).

[23] K. S. Markley, Fatty acids (1947).

PREPARATION AND STUDY OF PROPERTIES OF $\Delta^{2,3}$-DOCOSENOIC ACID

P. A. Artamonov

Unsaturated fatty acids of the docosenoic type, having the general formula $C_{22}H_{42}O_2$, appear to be incompletely studied. One of the more well known of these acids appears to be erucic acid ($\Delta^{13,14}$-docosenoic acid) which occurs combined in vegetable oils of the mustard family (mustard oil, rapeseed oil, rape oil). Erucic acid was first prepared by Darby [1] and its structure was established by Filety [2]. Cetoleinic acid ($\Delta^{11,12}$-docosenoic acid) is less well known. This acid was first prepared by Toyama [3] who also demonstrated its structure. Several other docosenoic acids have been prepared synthetically, but their structures have not been definitely established. For instance, two isomeric acids — 8-docosene-22-oic and 10-docosene-22-oic — were reported obtained by hydrogenation of erucic acid methyl ester at 200° [4]. The preparation by synthesis of the isoacid 1-docosene-22-oic acid has been reported [5]. Aleksandrov and Zaitsev [6] described an acid prepared by action of an alcoholic solution of potassium hydroxide on iodobehenic acid. The acid they required was prepared by reaction of phosphorous tri-iodide on erucic acid. The "isoerucic" acid they prepared had an m.p. of 54-56°. In the opinion of several investigators [7,8], this acid is entirely similar to erucic acid. Opinions exist [9, 10] that isoerucic acid as prepared by Aleksandrov and Zaitsev is not a pure substance but rather a mixture of acids. The remaining acids of this group have not been studied at all.

EXPERIMENTAL

As raw material for preparation of $\Delta^{2,3}$-docosenoic acid, we used chemically pure behenic acid. Behenic acid with an 81° m.p. was obtained by hydrogenation of chemically pure erucic acid separated from rape oil. α-Brombehenic acid was prepared from behenic acid by methods reported in our previous papers [11, 12].

By the bromination of 250 g behenic acid, 296 g pure α-brombehenic acid was obtained with an m.p. of 70-70.5°, which agrees with the literature value [13]. The yield of α-brombehenic acid was 95-96% of that theoretically possible.

0.2500 g substance: 0.1113 g AgBr (Stepanov). 0.1775 g substance: 0.0783 g AgBr. Found %: Br 18.94, 18.77. $C_{22}H_{43}O_2Br$. Calculated %: Br 19.08.

α-Brombehenic acid was a lustrous fluffy mass of needle-shaped crystals. It was readily soluble in many organic solvents (alcohol, chloroform, acetone, petroleum ether). It crystallized well from petroleum ether. $\Delta^{2,3}$-Docosenoic acid was prepared from α-brombehenic acid.

100 g α-brombehenic acid was placed in a porcelain dish, 240 ml of a 30% alcoholic solution of chemically pure potassium hydroxide was added, and the mixture heated on a vigorously boiling water bath, for 2.5-3 hours, until the alcohol was completely vaporized. The saponified mass was made into a pasty slurry with water and weakly acidified with sulfuric acid (10%). The supernatent fatty material was readily separated from the water layer, washed once with distilled water, and extracted with ethyl ether. The ether solution was dried with calcium chloride and the ether vaporized, yielding 78.6 g of a waxy light yellow solid residue.

In order to study its composition, this latter was fractionally separated using solvents. We assumed that the solid residue was a mixture of ethoxyacids, hydroxyacids, and unsaturated acids, and by analogy with products we had obtained through action of caustic on α-bromstearic acid [11] or an α-brompalmitic acid [12], it was decided first to separate α-hydroxybehenic acid which, according to the literature, melts at 96-97° and is not soluble in petroleum ether. For this purpose the mixture of acids was pulverized as finely as possible and dissolved in petroleum ether in the ratio of 1:10 with gentle heating on a water bath. The insoluble portion of the residue, which we assumed to be α-hydroxybehenic acid, was separated from the filtrate and washed three times with petroleum ether on a Shott funnel. The residue obtained had a 94.5-95° m.p. (Fraction 1). The filtrate from the first separation was cooled to 0°, producing a characteristic crystalline precipitate which was readily separated from the

filtrate by low temperature filtration. This second precipitate weighed 3.8 g, m.p. 71-72° (Fraction 2). The filtrate from the second separation was further cooled to minus 3-5°. A copious dense precipitate of finely crystalline material, having an m.p. of 56-57° was obtained (Fraction 3).

| Run No. | Quantity of | | Fraction Number | | | | | |
| | α-brombe-henic acid used (in grams) | Solid residue resulting from debromination of α-brombe-henic acid (g) | 1 | | 2 | | 3 | |
			Grams	%	Grams	%	Grams	%
1	100	79.6	18.6	23.37	3.6	4.6	56.7	71.2
2	100	80.5	12.1	14.70	3.8	4.7	63.2	78.4
3	50	40.0	4.4	11.0	2.5	5.5	32.4	81.0

The results of three runs in which alcoholic caustic was reacted with α-brombehenic acid and the reaction products fractionally separated are given in the table.

Assuming that the unsaturated docosenoic acid occurred in Fraction 2, we combined the three portions of this fraction and obtained a material with m.p. 71-72° which was used for further study.

Investigation of Fraction 2. Making the assumption that this fraction consisted of unsaturated $\Delta^{2,3}$-docosenoic acid contaminated with admixtures (hydroxy- and ethoxy-acids), the material was repeatedly fractionally crystallized from petroleum ether and chloroform in order to purify it. This resulted in a pure product with m.p. 68.5-69°.

0.1680 g substance: 0.4799 g CO_2; 0.1852 g H_2O. 0.1468 g substance: 0.4198 g CO_2; 0.1614 g H_2O. Found %: C 77.90, 78.0; H 12.34, 12.31. $C_{22}H_{42}O_2$. Calculated %: C 78.02; H 12.51.

Determination of acid number. 0.2176 g substance: 6.4 ml 0.1 N KOH 0.2240 g substance: 6.6 ml 0.1 N KOH Found: acid number 165.03, 165.32. $C_{22}H_{42}O_2$. Calculated: acid number 165.72. The iodine number was determined by the Hübl method, and amounted to 18.75 * (theoretical 74.98).

For further study, our product was given a saturation hydrogenation and yielded behenic acid melting at 81°.

The above data demonstrated that we were dealing with an individual unsaturated docosenoic acid.

In order to establish the location of the double bond in the molecular structure of the acid under study, we subjected it to oxidative cleavage using potassium permanganate in alkaline medium. The oxidation procedure is described in our previous paper on the synthesis of $\Delta^{2,3}$-hexadecenoic acid. From the oxidation we obtained a product, having a 75.5° m.p., which after three recrystallizations from ethyl alcohol had an m.p. of 76.2°. This resulting material evidently was arachidic acid.

0.2004 g substance: 0.5631 g CO_2; 0.2300 g H_2O. 0.1800 g substance: 0.5068 g CO_2; 0.2086 g H_2O. Found %: C 76.63, 76.78; H 12.85, 12.97. $C_{20}H_{40}O_2$. Calculated %: C 76.84; H 12.91.

Determination of acid number. 0.1615 g substance: 5.15 ml 0.1 N KOH 0.1776 g substance: 5.70 ml 0.1 N KOH Found: acid number 178.92, 180.08. $C_{20}H_{40}O_2$. Calculated: acid number 179.65. The iodine number of the resulting product was zero.

Judging from all the above data, we may assert that the product obtained was actually arachidic acid — $C_{20}H_{40}O_2$. Furthermore, a sample mixed with arachidic acid did not melt at a lower temperature.

Consequently, the unsaturated acid appears to be $\Delta^{2,3}$-docosenoic acid with the following structure: $CH_3(CH_2)_{18}CH=CHCOOH$.

Preparation of salts of $\Delta^{2,3}$-docosenoic acid. The silver salt of $\Delta^{2,3}$-docosenoic acid was prepared by us by a double decomposition reaction; we heated 0.1 N silver nitrate solution and an alcoholic solution of the potassium salt of the acid under study. The silver salt thus obtained was a gray crystalline powder with a 154-155° m.p.

0.1604 g substance: 0.3461 g CO_2; 0.1342 g H_2O; 0.0387 g Ag. 0.1764 g substance: 0.3834 g CO_2;

* α - and β-unsaturated acids characteristically give reduced iodine numbers.

0.1454 g H_2O; 0.0430 g Ag. Found %: C 58.85, 59.28; H 9.36, 9.23; Ag 24.12, 24.38. $C_{22}H_{41}O_2Ag$. Calculated %: C 59.30; H 9.28; Ag 24.23.

The lead salt of $\Delta^{2,3}$-docosenoic acid was prepared by double decomposition of lead acetate and the sodium salt of the acid under study in an alcoholic medium with heating. Some of the salt prepared was used for a determination of lead content, and the following results were obtained: 0.2004 g substance: 0.0688 g $PbSO_4$. Found %: Pb 23.45. $(C_{22}H_{42}O_2)_2Pb$. Calculated %: Pb 23.49. The lead salt $\Delta^{2,3}$-docosenoic acid was a white crystalline powder melting at 105°.

Preparation of $\Delta^{2,3}$-docosenoic acid ethyl ester. The ethyl ester of $\Delta^{2,3}$-docosenoic acid was prepared by esterification of the acid with ethyl alcohol in presence of sulfuric acid. 2 g pure $\Delta^{2,3}$-docosenoic acid and 20 ml absolute alcohol were placed in a small flask, (50 ml volume); 4 ml concentrated sulfuric acid were added to the mixture. The resulting mixture was heated on a water bath for a period of 30-45 minutes.

The separated ester of $\Delta^{2,3}$-docosenoic acid $CH_3(CH_2)_{18}CH\!=\!CHCOOC_2H_5$, after removal from the acidic layer, was washed until neutral and crystallized from alcohol. After two recrystallizations it had an m.p. of 40-40.5°.

0.1856 g substance: 0.5362 g CO_2; 0.2060 g H_2O. 0.2042 g substance: 0.5880 g CO_2; 0.2284 g H_2O. Found %: C 78.80, 78.45; H 12.43, 12.52, $C_{22}H_{41}OOC_2H_5$. Calculated %: C 78.62; H 12.66.

Investigation of first and third fractions of product from reaction of alcoholic caustic on α-brombehenic acid. Fraction 1, separated from the reaction products and having an m.p. of 94.5° and insoluble in petroleum ether, appeared evidently to be α-hydroxybehenic acid. It was dissolved in chloroform by warming and crystallized, on cooling, as a fine lustrous prismatic crystalline material. After three recrystallizations from chloroform in the ratio of 1:6, the acid had a 96-97° m.p., which corresponds exactly with the literature value [13].

0.1806 g substance: 0.4904 g CO_2; 0.2023 g H_2O. 0.2709 g substance: 0.7336 g CO_2; 0.2984 g H_2O. Found %: C 74.05, 73.85; H 12.54, 12.33. $C_{22}H_{44}O_3$. Calculated %: C 74.08; H 12.45.

Determination of acid number 0.3118 g substance: 8.8 ml 0.1 N KOH 0.1563 g substance: 4.4 ml 0.1 N. KOH Found: acid number 158.35, 157.96. $C_{22}H_{44}O_3$. Calculated: acid number 157.44.

Determination of hydroxyl number, by Normann method [14]. 0.9640 g substance: 4.9 ml 0.5 N KOH. 0.8676 g substance: 4.4 ml 0.5 N KOH. Found: hydroxyl number 142.54, 139.04. Calculated: hydroxyl number 140.85. Number of hydroxyl groups: 1.01, 0.99.

On the basis of the data obtained we may conclude that the substance studied in Fraction 1 actually is α-hydroxybehenic acid with the structure: $CH_3(CH_2)_{19}CHOHCOOH$.

Fraction 3, separated from the reaction products with an m.p. of 56-57°, after repeated recrystallizations from petroleum ether had a 60-60.5° m.p. This substance, as has been mentioned above, appears to be α-ethoxybehenic acid and has, consequently, the following structure: $CH_3(CH_2)_{19}CH(OC_2H_5)COOH$.

0.3216 g substance: 0.8836 g CO_2; 0.3561 g H_2O. 0.2464 g substance: 0.8114 g CO_2; 0.2794 g H_2O. Found %: C 75.06, 74.82; H 12.40; 12.72. $C_{24}H_{48}O_3$. Calculated %: 74.92; H 12.58.

Determination of acid number. 0.1800 g substance: 4.85 ml 0.1 N KOH 0.1880 g substance: 4.9 ml 0.1 N. KOH Found: acid number 145.62, 146.23. Calculated: acid number 145.93.

SUMMARY

1. $\Delta^{2,3}$-docosenoic acid has been prepared in the chemically pure state and its structure established. Silver and lead salts as well as the ethyl ester of this acid were prepared.

2. In the action of alcoholic caustic on α-brombehenic acid, some 70-80% of the material reacts to form α-ethoxybehenic acid, approximately 11-23% goes to α-hydroxybehenic acid, and only 4.5-5.5 % forms $\Delta^{2,3}$-docosenoic acid.

LITERATURE CITED

[1] S. Darby, Ann., 69, 1 (1849).

[2] M. Filety, J. prak. Chem., (2) 48, 72 (1893); (2) 48, 323 (1893).

[3] G. Toyama, J. Soc. Chem. Ind. Japan, 30, 597 (1927).

[4] T. Hilditch and N. Vidyarthi, Proc. Roy. Soc., (A) 122, 555-552.

[5] L. Ruzicka, M. Stoll and H. Schinz, Helv. Chem. Acta, I, 682 (1928).

[6] Aleksandrov and N. Zaitsev, J. pr. Ch., (2) 49, 58 (1894); (1) 50, 58 (1894).

[7] G. Ponzio, Gazz., 34, II, 50 (1904).

[8] L. Mascarelly et Tosch. Gazz.chim. Ital. 45, I, 313 (1915); 45, II, 335 (1915).

[9] Y. Mirchandam and Simenson, J. Chem. Soc., 1927, 371.

[10] A. Ralston, Fatty Acids and their derivatives, 1948.

[11] G. Pigulevsky and P. Artamonov, J. Gen. Chem. 12, nos. 9-10 (1942).

[12] P. Artamonov, J. Gen. Chem. 22, 1988* (1952)

[13] M. Filety, Gazz chim. Ital., 27, 11, 298 (1897).

[14] W. Normann, Fettchemische Umschau, 10, 194-196 (1933).

BORON TRIFLUORIDE AS A CATALYST IN ORGANIC CHEMISTRY

VI. REACTION OF O-CHLORPHENOL WITH CYCLOHEXANE

S. V. Zavgorodny

Alkylhalophenols and alkyl halophenyl ethers, according to the literature, have powerful germicidal and insecticidal activity and consequently are of definite interest. They are prepared, usually by halogenation of alkylphenols or alkyl phenyl ethers, and less often by reaction of alcohols or alkyl halides on halophenols. Direct alkylation of halophenols by olefins has hardly been studied. * Continuing our study on alkylation of phenols by olefins, we investigated the reaction of o-chlorphenol and cyclohexene in presence of boron trifluoride ethyl etherate as a catalyst. The reaction was studied at room temperature (16-20°) and at 95-97° using various ratios of reactants. Quantity of catalyst employed was 3-4%. It was established that o-chlorphenol reacts with cyclohexene in presence of $BF_3 \cdot O(C_2H_5)_2$ even at room temperature. Heating the reaction mixture on a boiling water bath significantly increased reactivity, so that the same results were obtained with 2 hours heating on a water bath as had been obtained in 15 days standing of the reaction mixture at room temperature. Increase in length of heating within the limits of 2-8 hours also increased yield of reaction products. However, along with this higher temperature and increased length of reaction time there is a higher degree of polymerization of cyclohexene.

It is noteworthy that for the conditions explored by us (room temperature for 15 days and 95-97° for 8 hours) the sole reaction products appeared to have been etheric compounds. At room temperature, cyclohexyl o-chlorphenyl ether was the only product and almost no polymerization of cyclohexene occurred. As regards phenolic type compounds, their formation under our stated conditions was not observed, at least not in quantities which could be separated by distillation from unreacted o-chlorphenol. Doubling the quantity of cyclohexene reduced reaction velocity at room temperature and reduced the yield of cyclohexyl o-chlorphenyl ether from 48% to 36% for the same length of time. However, at boiling water bath temperature, the ether yield increased from 73% to 79% (in 8 hours).

The extreme stability of cyclohexyl o-chlorphenyl ether toward isomerization also deserves mention. We found that this ether in presence of 25% $BF_3 \cdot O(C_2H_5)_2$ did not isomerize when heated for 8 hours at 120-140°, and in this connection may be fully compared with anisole and phenetole. This appears to be the main reason for the absence of expected phenolic compounds in our products, because they are usually formed by isomerization of alkyl phenyl ethers.

EXPERIMENTAL

We used freshly distilled commercial o-chlorphenol; it was a colorless liquid with a characteristic clinging odor and had b.p. 172-173°: d_{20}^{21} 1.2428. Cyclohexene was prepared by dehydration of cyclohexanol [3]. B.p. 82°; d_{20}^{21} 0.8137. Boron trifluoride ethyl etherate used was freshly distilled at 124-127°.

The reaction was carried out in flasks, having 60 ml volume, into which was weighed o-chlorphenol, catalyst, and finally cyclohexene. On shaking, reactants and catalyst mixed well without significant warming and formed a homogenous almost colorless liquid which rapidly turned light-orange.

On standing the mixture's color became progressively darker, and after 15 days the liquid became dark and opaque although quite limpid. After 2 hours heating on a boiling water bath, the mixture became opaque and after 8 hours heating was converted into a black-colored viscous mass.

After elapse of the specified heating time or the time of standing at room temperature, the reaction

---

* After this research was concluded, a paper appeared which described alkylation of o-chlorphenol and p-bromphenol with isobutylene and cyclohexene [1,2].

mixture was steam distilled. This vaporized unreacted o-chlorphenol and cyclohexene, lower polymers of cyclohexene and some (very little) of the cyclohexyl o-chlorphenyl ether. The ether product together with polymerized cyclohexene remained in the flask; depending on the test conditions this material was a light-yellow limpid liquid with a lemon odor (runs 1 and 5), a heavy brown oil (run 2), a quite transparent but rather viscous mass (run 3), or a yellow porous semi-solid difficult to separate from water (run 4). For complete removal of phenolic compounds, this material was treated with 10% soda solution, washed with water, dissolved in ether, dried with potash, and vacuum distilled.

Materials taken overhead in the steam distillation were similarly washed with soda solution. This dissolved phenolic compounds. After springing from the alkaline solution by hydrochloric acid, these distilled below 200° and appeared to be unreacted o-chlorphenol. The soda solution insoluble fractions obtained in the first four runs were combined for distillation; corresponding fractions of the last two runs were distilled separately. This material appeared mainly to be unreacted cyclohexene together with a mixture of polymers and ether. All data are given in the table.

In order to identify the etheric compounds prepared, having close boiling point and specific gravity they were recombined and distilled a second time. On distillation of the combined first product fractions, as given in the table, cyclohexyl o-chlorphenyl ether, boiling at 167-170° at 16-17 mm, was separated as the main and practically only product.

d_4^{16} 1.1260; n_D^{16} 1.5489; MR_D 59.47; calculated 58.32. 13.99 mg substance: 35.31 mg CO_2; 9.38 mg H_2O. 8.64 mg substance: 21.83 mg CO_2; 5.87 mg H_2O. 0.1602 g substance: 0.1055 g AgCl. Found %: C 68.88, 68.95; H 7.53, 7.56. Cl 16.29. $C_{12}H_{15}OCl$. Calculated %: C 68.38; H 7.18; Cl 16.83.

Reaction of o-chlorphenol with cyclohexene in presence of borontrifluoride ethyletherate

Run No.	Reaction feed (grams)			Reaction conditions		Ether product - not vaporized in steam distillation					Vaporized in steam distillation	
	o-chlor-phenol	cyclo-hexene	$BF_3 \cdot O(C_2H_5)_2$	Temper-ature	Time	Total yield before distillation		Obtained after distillation			Insoluble alkali (grams)	Soluble in alkali (g)
						Grams	%	(g)	B.p.mm	d_{20}^{24}		
1	12.20	8.97	0.97	16-20°	15 days	9.67	48.11	8.30	155-57° (15-16)	1.1191	3.95	1.88
2	11.91	7.91	0.83	16-20	24 hrs.	9.75	49.90	5.68	155-80° (17-18)	1.1225	2.80	3.46
				95-97	2 hrs.			3.21	240-75° (15)			
3	11.99	7.81	0.82	95-97	4 hrs.	11.37	56.52				1.80	1.70
4	12.10	8.10	0.93	95-97	8 hrs.	12.48	62.93	5.30	150-68° (12)	1.1276	1.80	2.58
								3.60	215-54° (12)			
5	12.07	16.45	0.91	16-20	15 days	7.20	36.38	4.24	157-65° (16-17)	1.1176	16.20	1.30
6	12.18	14.88	0.91	95-97	8 hrs.	15.77	78.97	—	170-95° (17) 245-84° (15)	1.1172	9.20	2.00

The ether was a transparent colorless liquid with a pungent floral odor.

A small amount of material having b.p. 160-166° at 16-17 mm; d_4^{15} 1.1088; n_D^{15} 1.5454; was also separated; its chlorine content was somewhat low and its carbon and hydrogen contents high, compared with calculated values for cyclohexyl o-chlorphenyl ether.

From steam distillation overhead products which were insoluble in alkali, we separated by a second distillation the dimer of cyclohexene, having b.p. 110-133° at 15-16 mm; d_{20}^{24} 0.9662; n_D^{20} 1.5227; molecular weight 169.4.

Isomerization of cyclohexyl o-chlorphenyl ether in presence of boron trifluoride ethyl etherate. 3.42 g cyclohexyl o-chlorphenyl ether having b.p. 167-170° at 16-17 mm was mixed in a test tube with 0.85 g boron trifluoride ethyl etherate. The tube was sealed and heated for 8 hours at 120-140°. After cooling the tube was opened and the mixture treated with a 5% aqueous sodium hydroxide solution. The cyclohexyl o-chlorphenyl ether taken for the test was quantitatively recovered. The same result was also obtained for the product having a b.p. of 160-166°. Consequently, cyclohexyl o-chlorphenyl ether does not isomerize in the presence of $BF_3 \cdot O(C_2H_5)_2$ under the conditions of our test, and therefore, cyclohexylphenols were not separated.

SUMMARY

1. o-Chlorphenol and cyclohexene react at room temperature in presence of boron trifluoride ethyl etherate to form cyclohexyl o-chlorphenyl ether only.

2. At boiling water bath temperatures polymerization of cyclohexene occurs to a considerable degree together with formation of cyclohexyl o-chlorphenyl ether.

3. Cyclohexyl o-chlorphenyl ether appears to be a compound of considerable stability and does not isomerize in presence of boron trifluoride ethyl etherate when heated at 120-140° for 8 hours.

LITERATURE CITED

[1] P. Levas, Ann. chim. et phys., 3, 145 (1948).

[2] H. Hart, J. Am. Chem. Soc. 71, 1966 (1949).

[3] Synthesis of Organic Preparations, 1, 240 (1932).
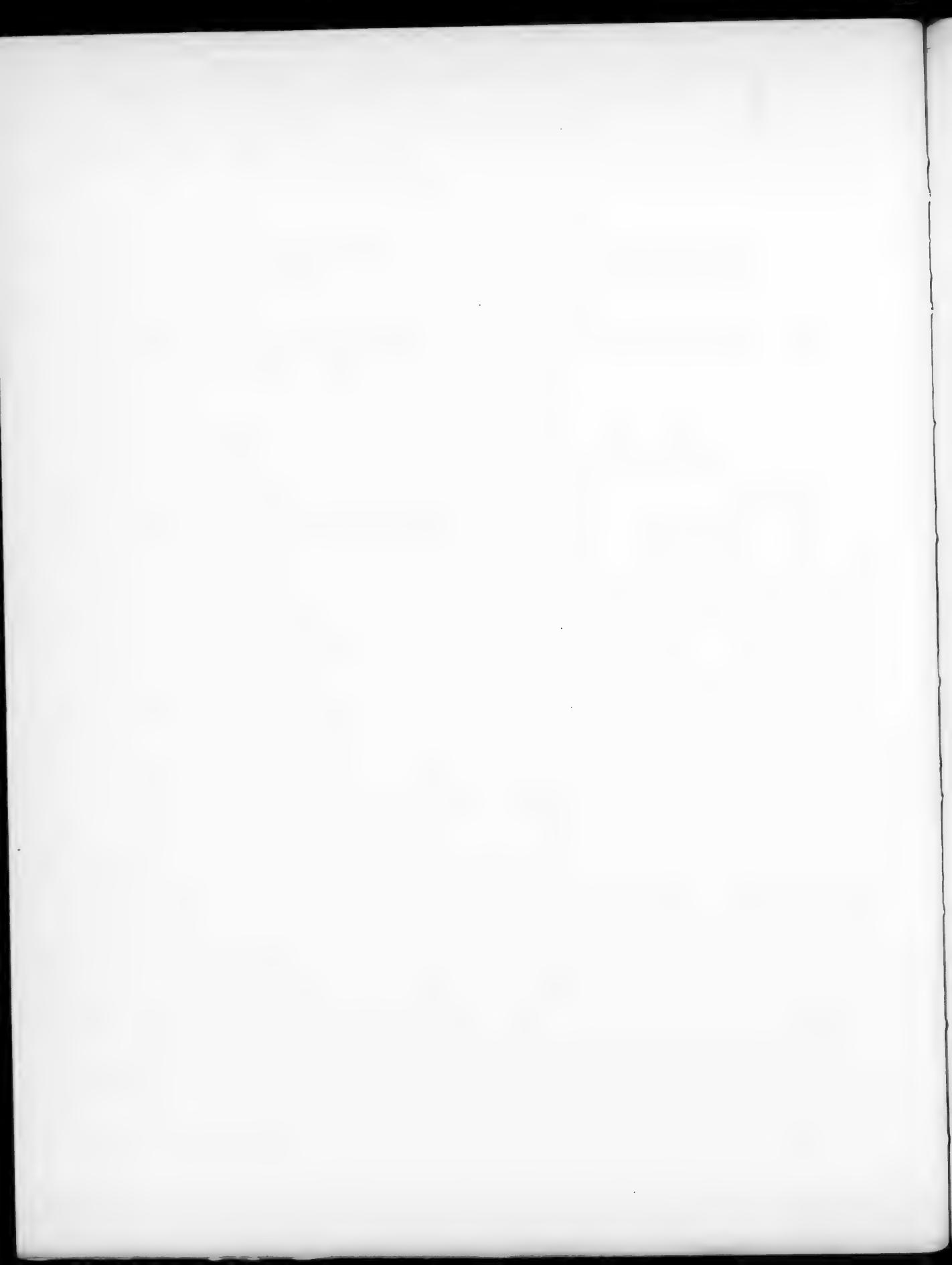
DERIVATIVES OF ZINGERONE

V. DERIVATIVES OF RESORCINOL

A. Ya. Berlin and .T. P. Sicheva

Our earlier papers on synthesis of derivatives of zingerone [1-4] led to a number of relationships between chemical structure and physiological activity for substances having structure similar to 4-hydroxy-3-methoxy-phenylethyl methyl ketone (zingerone):
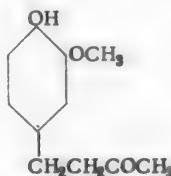
An unanswered question which developed during this work was whether physiological activity of compounds similar to zingerone depended on the relative positions of the hydroxyl and methoxyl groups on the benzene ring. In connection with this we became interested in synthesizing a group of compounds having structural similarity to zingerone, but in which the hydroxyl group would be meta to the methoxyl group and both would be in the 2 and 4 positions with respect to the side chain. The formulas given below show all possible structures for this group of compounds:
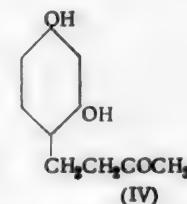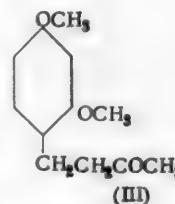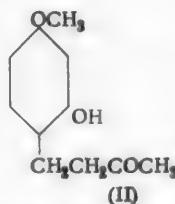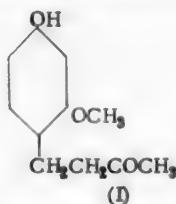
By analogy with the zingerone synthesis, we used the following sequence of syntheses to prepare these compounds:

($R = H$ or CH_3).
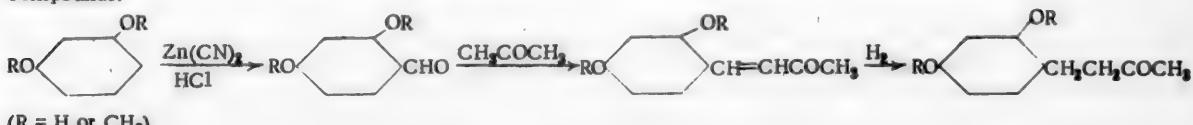
Resorcinol was used as a starting material, and its dimethyl or monomethyl ethers were prepared by methylation with dimethyl sulfate. In preparation of the corresponding aldehydes, we found that 2-methoxy-4-hydroxyl-benzaldehyde and 2-hydroxy-4-methoxybenzaldehyde, necessary for synthesis of compounds (I) and (II), were formed simultaneously in almost quantitative yield by action of zinc cyanide on resorcinol monomethyl ether in presence of dry hydrogen chloride. 2,4-Dimethoxybenzaldehyde has been prepared by a similar procedure from resorcinol dimethyl ether, but using aluminum chloride [5]. The aldehydes were condensed with acetone at room temperature in water or in aqueous alcohol in presence of caustic. Hydrogenation of resulting styryl ketones took place smoothly using skeletal nickel catalyst and yielded the corresponding substituted phenylethyl methyl ketones. Using palladium black the reaction is not well-defined and a mixture is obtained containing more completely hydrogenated products.

We experienced considerable difficulty in attempting synthesis of 2,4-dihydroxyphenylethyl methyl

ketone (IV). The literature contains indications that benzaldehyde with two ring hydroxyl groups does not condense with acetone [2,6]. Our work confirmed this. It appeared probable to us that 2,4-dihydroxyphenylethyl methyl ketone could be made by demethylation of previously prepared 2-methoxy-4-hydroxyphenylethyl methyl ketone. We performed a series of tests on dimethylation of this compounds under widely different reaction conditions: hydrobromic acid in glacial acetic acid, aluminum chloride in benzene, aluminum chloride in nitrobenzene, heating with aniline hydrochloride, and heating with mixed sulfuric and glacial acetic acids. All these tests resulted in a tarry reaction product from which it was not possible to separate individual substances. Evidently, this may be explained, on the one hand, by the extreme instability of dihydroxyphenylethyl methyl ketone having a hydroxyl group ortho to the side chain, and on the other, by possible enolization of the carbonyl group which could lead to formation of highly condensed cyclic compounds [2] and tars under these relatively severe conditions which are normally employed for saponfication of methyl phenyl ethers. In consequence, we were forced to explore other procedures for synthesis of 2,4-dihydroxyphenylethyl methyl ketone. The problem was whether we could find a substitute for the hydroxyl groups of resorcylaldehyde, which would not be affected during the condensation reaction with acetone carried out in an alkaline medium, but which, nevertheless, could then be readily split off under mild conditions. The benzyl group appeared to us most satisfactory for this purpose. It could be expected that catalytic hydrogenation of the benzyl ether of dihydroxystyryl ketone would lead to splitting off the benzyl groups as toluene at the same time the double bond became saturated. The similar splitting of benzyl groups from nitrogen or sulfur by catalytic hydrogenation is well known. However, cleavage of benzyl ethers under these conditions has been considerably less investigated, although there are references to the use of palladium on carbon for catalytic hydrogenation of several benzyl ethers which were split with formation of toluene and hydroxycompounds [7,8]. Because use of palladium as a catalyst might cause reduction of the carbonyl group, we decided to employ a skeletal nickel catalyst, not used heretofore for cleavage of benzyl ethers. We hydrogenated 4-benzyloxy-2-hydroxystyryl methyl ketone (prepared by condensation of 4-benzyloxy-2-hydroxybenzaldehyde [9] with acetone) in absolute alcohol at room temperature and atmospheric pressure. The quantity of hydrogen necessary for reduction of the double bond was very rapidly absorbed; the balance of the absorption process took place very slowly. The reaction yielded a thick yellowish uncrystallizable oil which could not be distilled even at a 0.2 mm vacuum without substantial decomposition. Consequently, the analyses on the fraction obtained were not wholly satisfactory; however, they were quite adequate to demonstrate that complete removal of benzyl groups by hydrogenation had occurred. Another confirmation of this was that more complete hydrogenation under the same conditions produced a crystalline colorless material, which, according to analyses, was 2,4-dihydroxyphenylethyl methyl carbinol.

In order to characterize most of the phenylethyl methyl ketones as well as several initial aldehydes and styryl ketones, their thiosemicarbazones were prepared.

Of the phenylethyl methyl ketones synthesized by us, only the 4-hydroxy-2-methoxy derivative had a very mild sharp taste; the other ketones did not have this property at all.

EXPERIMENTAL

Synthesis of 2-hydroxy-4-methoxyphenylethyl methyl ketone (II)

a) 2-Hydroxy-4-methoxybenzaldehyde. A mixture of 40 g zinc cyanide, 250 ml absolute ether, and 27 g resorcinol monomethyl ether was cooled in water containing ice; a rapid stream of dry hydrogen chloride was passed through the vigorously agitated mixture. During this period, solid zinc cyanide progressively disappeared and the aldimine hydrochloride began to separate as a thick rose-colored oil. Cooling was discontinued and subsequent flow of hydrogen chloride took place at room temperature. The reaction mixture was fully saturated with hydrogen chloride in 3-4 hours. The ether was decanted and the residual viscous mass washed with a small quantity of absolute ether and heated to boiling with 500 ml water. During this operation, the mass hydrolized and the solution became bright-red in color. On cooling the solution, a crystalline material separated which consisted of a mixture of 4-hydroxy-2-methoxybenzaldehyde and 2-hydroxy-4-methoxybenzaldehyde. Following separation of the precipitate by filtration, the filtrate was extracted several times with ether and the residue , recovered after vaporization of ether, was added to the main product portion. The aldehyde mixture was steam distilled. 2-Hydroxy-4-methoxybenzaldehyde was vaporized by the steam and condensed as a colorless oil which crystallized on cooling. Yield 10.2 g; m.p. 39-42° (according to the literature, the m.p. of 2-hydroxy-4-methoxybenzaldehyde is 42° [10].

Thiosemicarbazone —light-yellow crystals (from a mixture of acetone and water), m.p. 214° (with decomposition).

4.872 mg substance: 5.190 mg $BaSO_4$. Found %: S 14.63. $C_9H_{11}O_2N_3S$. Calculated %: S 14.22.

b) 2-Hydroxy-4-methoxystyryl methyl ketone. This was prepared by condensing 2-hydroxy-4-methoxy-benzaldehyde with acetone in aqueous caustic. The separated material melted at 125-126° (with decomposition). According to the literature, the m.p. of 2-hydroxy-4-methoxystyryl methyl ketone is 131° [11].

Thiosemicarbazone–grayish yellow crystals, decomposing on standing; m.p. 170-172°.

c) 2-Hydroxy-4-methoxyphenylethyl methyl ketone (II). 2 g skeletal nickel catalyst was added to a solution of 5 g 2-hydroxy-4-methoxystyryl methyl ketone in 100 ml absolute alcohol, and the mixture hydrogenated at room temperature and atmospheric pressure. After removal of catalyst and vaporization of solvent, the residue was vacuum distilled; during distillation the material decomposed and became violet-colored. A fraction boiling at 142-145° at 0.2 mm was collected; it was a colorless viscous liquid, readily soluble in alcohol and ether but insoluble in water.

4.870 mg substance: 12.077 mg CO_2; 3.139 mg H_2O. Found %: C 67.63; H 7.21. $C_{11}H_{14}O_3$. Calculated %: C 68.04; H 7.21.

Thiosemicarbazone –colorless crystals shaped like elongated prisms; m.p. 135-137°.

0.1319 g substance: 0.1125 g $BaSO_4$. Found %: S 11.78. $C_{12}H_{17}O_3N_3S$. Calculated %: S 11.98.

Synthesis of 2-methoxy-4-hydroxyphenylethyl methyl ketone (I)

a) 2-Methoxy-4-hydroxybenzaldehyde. 2-methoxy-4-hydroxybenzaldehyde was formed simultaneously with 2-hydroxy-4-methoxybenzaldehyde by action of zinc cyanide on resorcinol monomethyl ether in presence of hydrogen chloride (see above). The residue after steam distillation of 2-hydroxy-4-methoxybenzaldehyde was boiled with carbon; on cooling, 17 g 2-methoxy-4-hydroxybenzaldehyde (from 27 g resorcinol monomethyl ether) came out of solution as a crystalline lightly rose-colored material, m.p. 156-158° (according to the literature, m.p. of 2-methoxy-4-hydroxybenzaldehyde is 153° [10]).

Thiosemicarbazone –light yellow crystals (from aqueous alcohol), m.p. 196.5° (with decomposition).

5.471 mg substance: 5.546 mg $BaSO_4$. Found %: S 13.92. $C_9H_{11}O_2N_3S$. Calculated %: S 14.22.

b) 2-Methoxy-4-hydroxystyryl methyl ketone. To a solution of 4 g 2-methoxy-4-hydroxybenzaldehyde in a mixture of 48 ml 2.5% NaOH solution and 8 ml acetone, 12 ml 10% NaOH solution was added during the course of an hour followed by 120 ml water. The transparent dark red solution was allowed to stand at room temperature for two days and then diluted to 400 ml with water and cautiously acidified with hydrochloric acid until weakly acid to Congo Red. The bright-yellow crystals which separated were removed by filtration, washed with water, and dried in a vacuum desiccator. After recrystallization from aqueous alcohol using carbon, the substance had m.p. 165-166.5°. Yield 2.5 g.

4.248 mg substance: 10.763 mg CO_2; 2.411 mg H_2O. Found %: C 69.10; H 6.35. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.02.

Thiosemicarbazone –thick hexahedral plates (from 96% alcohol), m.p. 201-202° (with decomposition).

4.425 mg substance: 3.950 mg $BaSO_4$. Found %: S 12.26. $C_{12}H_{15}O_2N_3S$. Calculated %: S 12.07.

c) 2-Methoxy-4-hydroxyphenylethyl methyl ketone (I). 3 g skeletal nickel catalyst was added to a solution of 7.45 g 2-methoxy-4-hydroxystyryl methyl ketone in 75 ml 96% alcohol and the mixture hydrogenated at room temperature and atmospheric pressure. Absorption of hydrogen was complete in 20 minutes. After removal of catalyst, the solvent was vaporized by vacuum; and the residue crystallized. Material recrystallized from hot water using carbon had m.p. 116-118°; colorless prisms, readily soluble in alcohol and acetone, difficultly soluble in water. Yield 5.8 g.

3.301 mg substance: 8.202 mg CO_2; 2.191 mg H_2O. Found %: C 67.76; H 7.42. $C_{11}H_{14}O_3$. Calculated %: C 68.04; H 7.21.

Thiosemicarbazone –colorless plates (from aqueous alcohol), m.p. 176-178°.

4.559 mg substance: 4.060 mg $BaSO_4$. Found %: S 12.23. $C_{12}H_{17}O_3N_3S$. Calculated %: S 11.98.

Synthesis of 2,4-dimethoxyphenylethyl methyl ketone (III)

a) 2,4-Dimethoxybenzaldehyde was prepared by action of zinc cyanide on a benzene solution of resorcinol dimethyl ether in presence of hydrogen chloride and aluminum chloride [5]. M.p. 67-70° (according to the literature, m.p. of 2,4-dimethoxybenzaldehyde is 68-71° [5]).

Thiosemicarbazone — light yellow crystals (from aqueous alcohol), m.p. 194-195° (with decomposition).

5.178 mg substance: 5.035 mg $BaSO_4$. Found %: S 13.35. $C_{10}H_{13}O_2N_3S$. Calculated %: S 13.38.

b) 2,4-Dimethoxystyryl methyl ketone. 9.2 ml acetone and 14 ml 10% NaOH solution were added to a a solution of 4 g 2,4-dimethoxybenzaldehyde in 25 ml 96% alcohol. The mixture was allowed to stand for two days at room temperature. The liquid was then poured into 500 ml water; the thick dark yellow oil which separated was extracted using benzene. After drying the benzene solution and evaporation of solvent under vacuum, the residue was distilled at 2 mm; during distillation the material became considerably resinous and decomposed. A fraction (2.6 g) was separated having b.p. 185-190°, it was a thick, yellow oil.

Thiosemicarbazone of 2,4-dimethoxystyryl methyl ketone — spindle-shaped bright yellow crystals (from aqueous alcohol), m.p. 168-170°.

4.871 mg substance: 4.080 mg $BaSO_4$. Found %: S 11.50. $C_{13}H_{17}O_2N_3S$. Calculated %: S 11.47.

c) 2,4-Dimethoxyphenylethyl methyl ketone (III). A solution of 2.4 g 2,4-dimethoxystyryl methyl ketone in 50 ml absolute alcohol was hydrogenated in presence of skeletal nickel catalyst (1 g) at room temperature and atmospheric pressure. When hydrogenation was completed, the catalyst was removed by filtration, the solvent removed by distillation, and the residue — an uncrystallizable oily liquid — vacuum distilled. A fraction with b.p. 142-145° at 2 mm was obtained — colorless liquid, readily soluble in alcohol and acetone but insoluble in water.

3.218 mg substance: 8.164 mg CO_2; 2.196 mg H_2O. Found %: C 69.19; H 7.64. $C_{12}H_{16}O_3$. Calculated %: C 69.23; H 7.69.

Synthesis of 2,4-dihydroxyphenylethyl methyl ketone (IV)

a) β-Resorcyl aldehyde was prepared by action of zinc cyanide on an ether solution of resorcinol in presence of hydrogen chloride [12]. M.p. 136-137° (according to the literature, m.p. of β-resorcyl aldehyde is 135-136° [12]).

Thiosemicarbazone — fine, white needles (from 50% alcohol), m.p. 222.5° (with decomposition).

3.559 mg substance: 3.988 mg $BaSO_4$. Found %: S 15.38. $C_8H_9O_2N_3S$. Calculated %: S 15.16.

b) 4-Benzyloxy-2-hydroxybenzaldehyde. This was prepared by benzylation of 8 g resorcyl aldehyde using benzyl chloride in absolute alcohol in the presence of sodium alcoholate [9]. 2 g of a substance was obtained, m.p. 77-80° (according to the literature, m.p. of 4-benzyloxy-2-hydroxybenzaldehyde is 77-80° [9]).

Thiosemicarbazone — glistening thin plates (from alcohol), m.p. 210-211°.

6.865 mg substance: 0.846 ml N_2 (23°, 739.0 mm). Found %: N 13.81. $C_{15}H_{15}O_2N_3S$. Calculated %: N 13.95.

c) 4-Benzyloxy-2-hydroxystyryl methyl ketone. 4 ml acetone and 24 ml 2.5% NaOH solution were added to 3 g 4-benzyloxy-2-hydroxybenzaldehyde. A voluminous white precipitate of the sodium aldehyde derivative formed at once. To the resulting mass, 12 ml 10% NaOH solution was added, during the course of an hour, with stirring, followed by 50 ml water. The mixture was shaken for 60 hours, during which most of the mass slowly went into solution and the liquid developed an intense orange-red color. The remaining undissolved precipitate was removed by filtration, and the filtrate cautiously acidified with 2% hydrochloric acid solution until weakly acid to Congo red. The yellowish precipitate of styryl ketone was separated by filtration, dried, and washed twice with boiling petroleum ether to remove admixed initial aldehyde. After repeated recrystallization from 70% alcohol the material had m.p. 167°; lightly rose-tinted, elongated prisms readily soluble in acetone and boiling alcohol, insoluble in water. Yield 1.3 g.

3.101 mg substance: 8.602 mg CO_2; 1.593 mg H_2O. Found %: C 75.65; H 5.75. $C_{17}H_{16}O_3$. Calculated %: C 76.12; H 5.97.

From the sodium aldehyde derivative which did not enter the reaction, 1.6 g 4-benzyloxy-2-hydroxy-benzaldehyde was recovered.

d) Catalytic hydrogenation of 4-benzyloxy-2-hydroxystyryl methyl ketone. A solution of 1 g 4-benzyloxy-2-hydroxystyryl methyl ketone in 50 ml absolute alcohol was hydrogenated at room temperature and atmospheric pressure in presence of 1 g skeletal nickel catalyst. According to calculation, 186 ml H_2 (17°, 734 mm) is necessary for saturation of the double bond and removal of the benzyl group. The first 90 ml was absorbed very quickly, then hydrogenation became much slower, and finally absorption of hydrogen took place very slowly. After absorption of 200 ml hydrogen, the hydrogenation was stopped, catalyst filtered, solvent removed in vacuum, and the residue — a thick, yellowish liquid — vacuum distilled. During distillation the material became considerably resinous and decomposed, and it was not possible to achieve its complete purification. A fraction was separated with b.p. 175° at 0.3 mm which was a thick, non-crystalline yellow mass. The analytical data show that together with reduction of the double bonds, the benzyl group was almost completely removed while the carbonyl group remained unattacked.

5.969 mg substance: 14.969 mg CO_2; 3.757 mg H_2O. 4.227 mg substance: 1.06 ml CH_4 (17°, 737 mm). Found %: C 68.39; H 7.04; OH 17.51. $C_{10}H_{12}O_3$. Calculated %: C 66.66; H 6.66; OH 18.88.

Saturation hydrogenation under the same conditions gave a colorless crystalline material, m.p. 114-116°.

3.323 mg substance: 8.028 mg CO_2; 2.313 mg H_2O. Found %: C 65.89; H 7.77; $C_{10}H_{14}O_3$. Calculated %: C 65.70; H 7.69.

SUMMARY

1. We synthesized several zingerone-type compounds; they appear to be resorcinol derivatives having the hydroxyl and methoxyl groups in different positions of the benzene ring.

2. We found that all these compounds had practically no sharp taste.

LITERATURE CITED

[1] Berlin and Sherlin, J. Gen. Chem. 18, 1386 (1948).

[2] Berlin, Sherlin and Serebrennikova, J. Gen. Chem. 19, 569 (1949).*

[3] Berlin, Sherlin, and Serebrennikova, J. Gen. Chem. 19, 759 (1949).**

[4] Berlin and Markova, J. Gen. Chem. 19, 1567 (1949).***

[5] Adams, Montgomery, J. Am. Chem. Soc. 46, 1518 (1924).

[6] Buck, Heilbron, J. Chem. Soc. 1922, 1095.

[7] Morris, Riemenschneider, J. Am. Chem. Soc. 68, 500 (1946).

[8] Morris, J. Am. Chem. Soc. 71, 2056 (1949).

[9] Reichstein, Grussner, Helv. 18, 816 (1935).

[10] Kiewiet, Stephen. J. Chem. Soc. 1931, 84 .

[11] Heilbron, Whitworth, J. Chem. Soc. 1923, 244.

[12] Adams, Levine, J. Am. Chem. Soc. 45, 2373 (1923).

---

* See Consultants Bureau translation page 517.

** See Consultants Bureau translation page 739

*** See Consultants Bureau translation page 1579

SYNTHESIS OF 1-METHOXYPHENANTHRIDINE

A. Ya. Berlin and T. P. Sicheva

Monomethoxy substituted phenanthridines have not been reported in the literature until this time. While engaging in study of a group of derivatives of phenanthridine, we found it necessary to synthesize phenanthridine with a methoxyl group in the 1-position.

We planned to prepare this material by the following scheme:
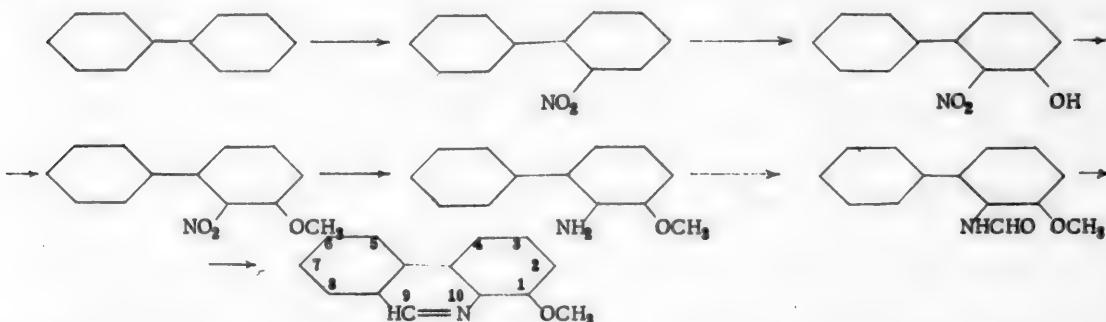
Biphenyl, the starting material for this synthesis, was prepared via phenyl magnesium bromide [1] with 85-95% yield.

We introduced the hydroxyl group into o-nitrobiphenyl by action of anhydrous potassium hydroxide in benzene solution [3]. It should be mentioned that this reaction was accompanied by considerable resin formation, which is associated, evidently, with the oxidation process, and it was not possible to obtain a satisfactory yield. By carrying out a series of experiments at different conditions, it was determined that the best yield of 2-nitro-3-hydroxybiphenyl (approximately 30% of theoretical) was obtained by performing the reaction at 90-95° over a 6-7 hour period; under these conditions a portion of the initial 2-nitrobiphenyl may be recovered.

We methylated 2-nitro-3-hydroxybiphenyl using dimethyl sulfate in caustic medium, yield was 90-96% of theoretical. The 2-nitro-3-methoxybiphenyl obtained was catalytically hydrogenated at atmospheric pressure and room temperature using skeletal nickel catalyst. Hydrogenation was performed both in alcohol and in ethyl acetate solution. In the latter, nitro group reduction took place considerably more rapidly and with quantitative yield of 2-amino-3-methoxybiphenyl.

By heating 2-amino-3-methoxybiphenyl with formic acid we prepared 2-formylamino-3-methoxybiphenyl, which was then subjected to ring closure using zinc chloride at 280-300° [4]. Considerable tar-formation occurred during ring-closure; we were able to separate only a very small amount of the base which was then converted to the picrate. In recrystallization of the picrate, two materials with different melting points and different crystalline forms were separated. Analytical data showed that they were the picrates of 1-hydroxy- and 1-methoxy-phenanthridine; from this it follows that the process of ring closure using zinc chloride leads to partial saponification of the methoxyl group.

The very small quantity of base separated from these picrates was purified by sublimation. Two materials were obtained thereby, which, according to the analytical data, were 1-hydroxyphenanthridine and 1-methoxyphenanthridine.

EXPERIMENTAL

2-Nitro-3-hydroxybiphenyl. A mixture of 3 g 2-nitrobiphenyl, 30 g finely subdivided potassium hydroxide, and 30 ml absolute benzene was agitated at 90-95° for 7 hours. After cooling, the dark red reaction mass was poured into water, the benzene layer separated, and the aqueous layer extracted several times with benzene. About 0.5 g of the initial 2-nitrobiphenyl were recovered from the benzene solution after removal of solvent.

The water layer was acidified with concentrated hydrochloric acid until acid to Congo red, and the dark oily precipitate which was formed extracted with ether. After removal of the ether, the residual dark tarry mass was repeatedly extracted with a saturated aqueous solution of sodium bicarbonate. This solution was acidified with hydrochloric acid; the dark crystalline precipitate which formed was removed by filtration, and dissolved in a small amount of ethyl alcohol; the resulting solution was diluted with three times its volume of water. Most of the tarry contaminants remained in solution in this step, and the precipitate which separated was almost pure 2-nitro-3-hydroxybiphenyl in the form of bright yellow crystals. Weight 1 g. After recrystallization from petroleum ether the material had m.p. 82-84° (according to the literature the m.p. of 2-nitro-3-hydroxybiphenyl is 81-82° [3]).

2-Nitro-3-methoxybiphenyl. To a hot bright red solution of 2.3 g 2-nitro-3-hydroxybiphenyl in 7 ml of 7% sodium hydroxide solution, was added 1.2 ml freshly distilled dimethyl sulfate and the mixture heated with agitation for 15 minutes; 17% sodium hydroxide solution was then added until alkaline. We continued, alternately adding dimethyl sulfate (0.5 ml portions) and caustic solution, until a red color no longer developed following the last addition of alkali (alkaline to litmus). A crystalline precipitate, which was extracted with ether, separated on cooling. The ether solution was washed with 2% sodium hydroxide solution, then with water, and dried with potassium carbonate. After evaporation of the solvent, a crystalline substance having m.p. 84-92° remained. Recrystallized from petroleum ether, 2-nitro-3-methoxybiphenyl had a m.p. of 101.5-102.5°. Weight 2.3 g (yield 95% of theoretical).

2.429 mg substance: 6.074 mg CO_2; 1.111 mg H_2O. 6.598 mg substance: 0.350 ml N_2 (20.5°, 729 mm). Found %: C 68.20; H 5.12; N 5.92. $C_{13}H_{11}O_3N$. Calculated %: C 68.12; H 4.80; N 6.11.

2-Amino-3-methoxybiphenyl. A solution of 3.9 g 2-nitro-3-methoxybiphenyl in 100 ml ethyl acetate was catalytically hydrogenated using skeletal nickel catalyst (5 g of paste). At end of reaction, catalyst was removed by filtration and solvent evaporated in vacuum. The residue was dissolved in ether, and the ether solution extracted with 2% hydrochloric acid solution. A dark-colored crystalline material was formed on evaporation of the acid solution. The weight of 2-amino-3-methoxybiphenyl hydrochloride was 4 g. The hydrochloride was dissolved in an excess of hydrochloric acid and the solution heated with carbon. After removal of carbon and addition of sodium hydroxide solution until alkaline, a white finely-crystalline precipitate was separated. On recrystallization from aqueous alcohol, 2-amino-3-methoxybiphenyl had m.p. 59-60.5°.

3.192 mg substance: 9.195 mg CO_2; 1.860 mg H_2O. 6.757 mg substance: 0.430 ml N_2 (19.5°, 725.0 mm). Found %: C 78.56; H 6.52; N 7.09. $C_{13}H_{13}ON$. Calculated %: C 78.39; H 6.53; N 7.03.

The picrate of 2-amino-3-methoxybiphenyl was prepared by addition of a saturated solution of picric acid in absolute ether to a solution of the amine in the same solvent. After recrystallization from water the substance had an m.p. of 153.5°.

3.428 mg substance: 0.395 ml N_2 (19.5°, 737.5 mm). Found %: N 13.04. $C_{13}H_{13}ON \cdot C_6H_3O_7N_3$. Calculated %: N 13.08.

2-Formylamino-3-methoxybiphenyl. A mixture of 2.5 g 2-amino-3-methoxybiphenyl and 5 ml freshly distilled formic acid was heated on an oil bath for 2 hours at 140°. Formic acid was then removed under vacuum; the residue was then ground with petroleum ether, whereupon the material crystallized. Crystals were removed by filtration, washed with petroleum ether, and dried. Weight 2.6 g. In order to remove unreacted amine, the material was dissolved in ether, and the ether solution extracted with 2% hydrochloric acid. After washing with water and removal of solvent, the residue was recrystallized several times from ether. Pure 2-formylamino-3-methoxybiphenyl had m.p. 113-114°.

7.660 mg substance: 3.38 ml 0.01 N H_2SO_4 (Kjeldahl). Found %: N 6.18. $C_{14}H_{13}NO_2$. Calculated %: N 6.16.

1-Methoxyphenanthridine. 2.4 g 2-formylamino-3-methoxybiphenyl and 6 g fused zinc chloride were placed in a round-bottom flask fitted with a thermometer reaching to the bottom and an air condenser. The mixture was heated on a Babo funnel for 6 hours at 240-290°. At the end of the reaction, the mass had turned very dark. The reaction mixture was treated with hot water, and the resulting greenish-brown precipitate was separated by filtration and treated with a 10% hydrochloric acid solution. A portion of the substance dissolved, but most of the material remained undissolved as a thick black tar. The acid solution was decanted from tar and poured into 25% aqueous ammonia to spring the free bases and to separate zinc remaining in the material.

A voluminous floculent precipitate was formed which was extracted with benzene. After evaporation of the solvent, the residue was heated for 15 minutes with 6 ml acetic anhydride in order to remove 2-amino-3-methoxybiphenyl, which could have been formed by hydrolysis of unreacted formyl derivative; the almost black solution was poured into 60 ml 1 N HCl.

The black tarry precipitate which separated was filtered, the filtrate made alkaline with 25% aqueous ammonia solution; during this a partially crystalline brown oil separated. It was extracted with benzene, and after evaporation of the solvent, the residue was dissolved in glacial acetic acid. A saturated solution of picric acid in glacial acetic acid was then added. The picrate, a voluminous yellow precipitate, was filtered, washed with glacial acetic acid, and dried in a vacuum dessicator. After repeated recrystallization from glacial acetic acid, we were able to separate the picrate into two different materials: 1-methoxyphenanthridine picrate and 1-hydroxyphenanthridine picrate.

The picrate of 1-methoxyphenanthridine formed fine curved needles, melting at 232°.

4.032 mg substance: 0.439 ml N_2 (18.5°, 748.0 mm). Found %: N 12.55. $C_{14}H_{11}ON \cdot C_6H_3O_7N_3$. Calculated %: N 12.78.

The picrate of 1-hydroxyphenanthridine formed elongated prisms, m.p. 219-220°.

3.376 mg substance: 0.406 ml N_2 (16.0°, 720.6 mm). Found %: N 13.48. $C_{13}H_9ON \cdot C_6H_3O_7N_3$. Calculated %: N 13.21.

Both prepared picrates were heated with concentrated hydrochloric acid. From the solution of hydrochlorides, the bases were separated in free form and purified by distillation.

1-Methoxyphenanthridine was separated from the picrate which melted at 232°; colorless crystals melting at 140-142°.

3.529 mg substance: 10.340 mg CO_2; 1.659 mg H_2O. 6.031 mg substance: 0.349 ml N_2 (18.0°, 748.5 mm). Found %: C 79.91; H 5.26; N 6.69. $C_{14}H_{11}ON$. Calculated %: C 80.38; H 5.26; N 6.69.

1-Hydroxyphenanthridine was separated from the picrate which melted at 219-220°; colorless crystalline substance melting at 186-188°.

4.219 mg substance: 12.301 mg CO_2; 1.791 mg H_2O. 6.008 mg substance: 0.372 ml N_2 (20.5°, 748.0 mm). Found %: C 79.52; H 4.75; N 7.09. $C_{13}H_9ON$. Calculated %: C 80.00; H 4.61; N 7.17.

SUMMARY

1-Methoxyphenanthridine and 1-hydroxyphenanthridine together with a group of new derivatives of biphenyl have been prepared and described.

LITERATURE CITED

[1] J. Krizewsky, Turner, J. Chem. Soc. 115, 559 (1919).

[2] Fortinsky, J. Russ. Chem. Soc. 44, 783 (1912) ; Bell, Kenyon, Robinson, J. Chem. Soc. 1242 (1929).

[3] A. Whol, Ber., 32, 3486 (1899); O. Derner, L. Drucker, Proc. Oklach. Acad. Sci. 23, 55 (1943); Chem. Abs. 2029 (1944).

[4] Morgan, Walls, J. Chem. Soc. 2229 (1932).

S. Ordzhonikidze All-Union Scientific Research
Inst. Pharm. Chem.
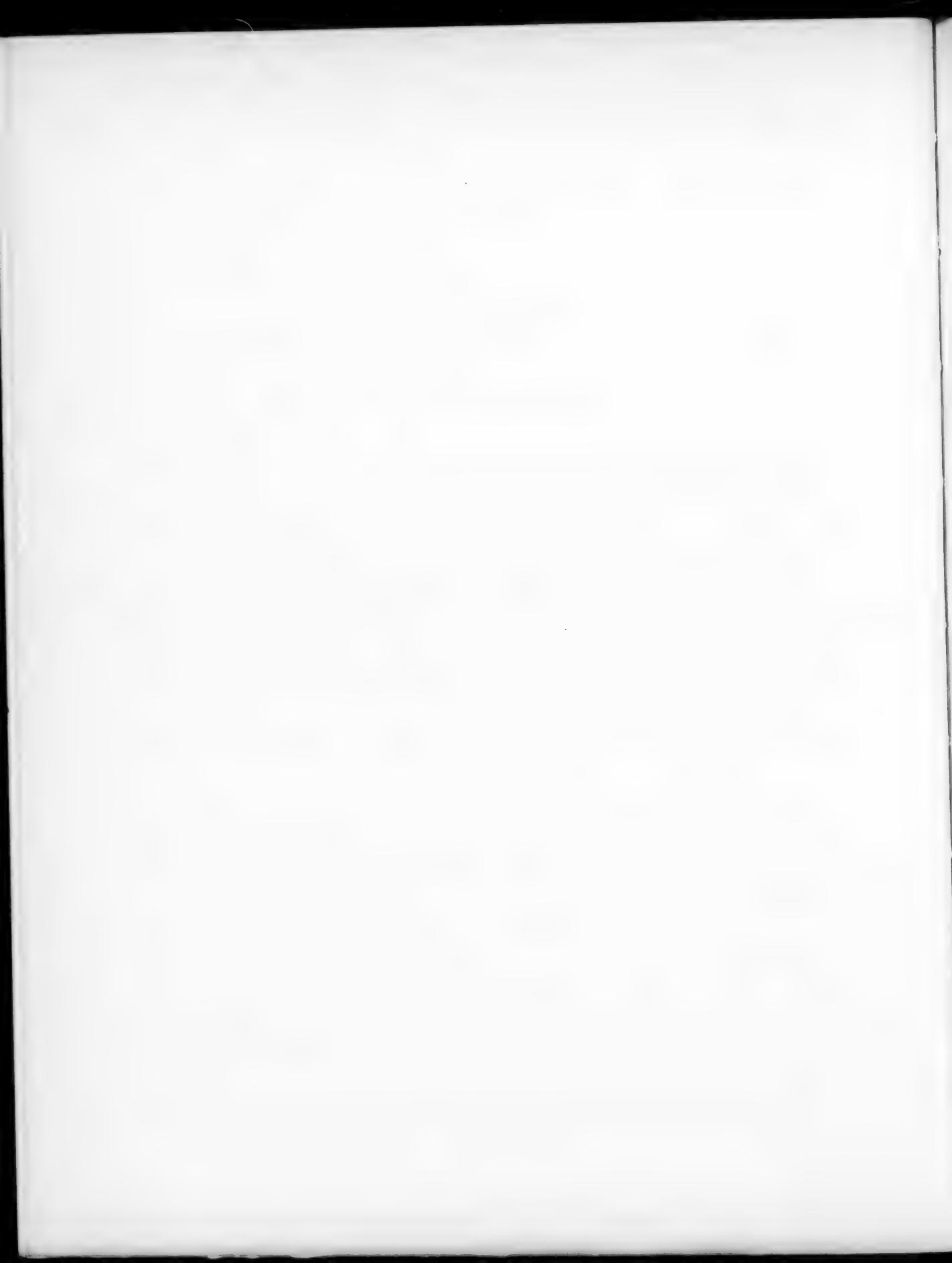
THE BETAINE-LIKE COMPOUNDS FORMED WHEN A PROTON IS DETACHED FROM THE NH-GROUP

VII. REACTION WITH ALKYL AND ACYL HALIDES

A. M. Simonov

The chemical properties of dipolar ions described in our earlier papers [1] have been studied comparatively slightly. We investigated the behavior of these compounds only with acids and water. It was shown that all dipolar ions of this type readily react with acids, even with dilute acetic acid, to form the corresponding quartenary salts. In contrast, hydration occurred only for those compounds we had prepared in whose molecules the nitrogen atom, bearing a negative charge, was linked to p-toluenesulfonic, benzoic, or p-nitrobenzoic acid radicals; in contact with water vapor, betaines of the stated structure added one, sometimes two, molecules of water relatively rapidly. Dipolar ions containing on the negatively charged nitrogen atom dinitrophenyl or picryl groups, i.e., groups which caused a particularly strong displacement of electrons from the negatively charged N-atom, were not converted into bases under the above stated conditions.

It is shown in this paper that dipolar ions of the type studied react with alkyl halides similarly to aminoacid betaines [2] and phenol-betaines of the quinoline type [3]. The alkyl group of the alkyl halide here attaches to the negative N-atom, and the reaction results in formation of a quartenary salt. For instance, methyl-betaine 6-(p-toluenesulfonamido)-quinoline (I) when heated readily combines with one molecule of methyl iodide; to the resulting compound must be attributed the structure of 6-(N-methyl-p-toluenesulfonamido)-quinoline methyl iodide (II), because it is identical to the quartenary salt formed by reaction of 6-(N-methyl-p-toluenesulfonamido)-quinoline (IV) with methyl iodide. Methylbetaine 6-methoxy-8-(p-toluenesulfonamide)-quinoline and methylbetaine 6-(2',4'-dinitroanilino)-quinoline react with methyl iodide in the same manner as does dipolar ion (I). The methyl ester of p-toluenesulfonic acid reacts with betaines in the same way as does methyl iodide.
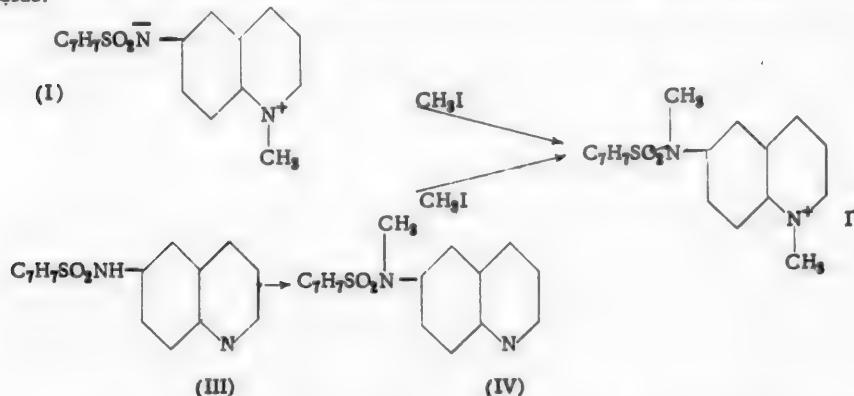
The reaction conditions are dependent on the nature of the radicals attached to the negatively charged N-atom. As in the case of hydration, the more electronophilic the group attached to the negative N-atom, the less readily is an alkyl group attached to that atom. For example, methyl-betaine-6-(p-toluenesulfonamido)-quinoline reacts with methyl iodide at 75-80°, while methylation of the structurally analogous betaine containing a 2,4-dinitrophenyl group instead of the p-toluenesulfonamido one proceeds satisfactorily only at the higher temperature of 125-130°.

The possibility of reaction between betaines of the type under study and acid chlorides is demonstrated using as an example reaction of methyl-betaine 6-(p-toluenesulfonamido)-quinoline (I) with benzoyl chloride; when heated at 120-130°, the quartenary salt (V) is formed.

(V)
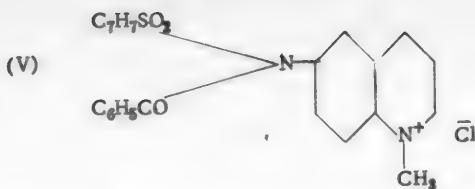
Returning to the question about alkylation of methyl-betaine 6-(p-toluenesulfonamido)-quinoline, we saw that it would be necessary to prepare 6-(N-methyl-p-toluenesulfonamido)-quinoline (IV) in order to explain the structure of the reaction product — quartenary salt (II). For this purpose, we attempted to methylate 6-(p-toluene-sulfonamido)-quinoline (III). The reaction did not give satisfactory yield, using ordinary methods of alkylation, because the alkylating agent primarily directs itself to the hetero N-atom, and in alkaline medium leads to formation of dipolar ion (I) or the free base corresponding to it. We therefore tried to perform the alkylation using trimethylphenylammonium hydroxide according to the Rodionov procedure [4]; this alkylation agent, successfully used for alkylation of phenols, shows special value in those cases where the compound to be alkylated has a tertiary N-atom, besides the phenolic hydroxyl group, which precludes the possibility of forming the quartenary salt (methylation of morphine). It could be expected that use of this alkylation procedure would be expedient in our case.

The possibility of methylating the —SO$_2$NH—group using trimethylphenylammonium hydroxide was first confirmed, with positive results, on the anilide of p-toluenesulfonic acid. The reaction goes according to the equation:

$$ArSO_2NHAr' + [C_6H_5N(CH_3)_3]OH \longrightarrow ArSO_2N(CH_3)Ar' + C_6H_5N(CH_3)_2 + H_2O.$$

In tests performed later to methylate by this procedure 6-(p-toluenesulfonamido)-quinoline, we were able to prepare 6-(N-methyl-p-toluenesulfonamido)-quinoline with a 60% yield, based on the anilide which was reacted. Consequently, quartenary ammonium bases may be successfully used to alkylate the NH-group of aryl sulfon-amides; this alkylation procedure is expedient, evidently, for those compounds whose molecules contain a tertiary nitrogen atom in addition to the substituted sulfonamide group.

In contrast with 6-(p-toluenesulfonamido)-quinoline, 8-(p-toluenesulfonamido)-quinoline and 6-methoxy-8-(p-toluenesulfonamido)-quinoline may be successfully alkylated using ordinary methods. The alkylating agent in these cases reacts primarily with the NH-group because quartenary salt formation takes place with difficulty; it is possible that this may be attributed to steric hindrance associated with presence of the toluenesulfonamido group in the 8-position, i.e, ortho to the hetero N-atom. The presence of a methyl group in position 8 has a similar influence, because methylation of 6-(p-toluenesulfonamido)-8-methylquinoline may also be performed using ordinary means [6].

EXPERIMENTAL

6-(N-Methyl-p-toluenesulfonamido)-quinoline. If the sodium salt of 6-p-toluenesulfonamidoquinoline was heated to 110° with the methyl ester of p-toluenesulfonic acid, the formation of a brown tarry product together with copious gas evolution was observed; probably, a betaine was first formed which then decomposed under the reaction conditions. By performing the alkylation under milder conditions, for instance by heating 6-p-toluene-sulfonamidoquinoline with the methyl ester of p-toluenesulfonic acid in acetone solution in presence of potassium carbonate, considerable betaine-formation takes place; the yield of N-methyl derivative as a contaminant is very small. Alkylation using dimethyl sulfate in cold aqueous alkaline solution gave the base almost exclusively. Satisfactory results were obtained only by alkylation with trimethylphenylammonium hydroxide, following Rodionov [4]. An equimolar quantity of alkylating agent was used in the reaction.

0.23 g sodium was dissolved in 5 ml alcohol; to the alcoholate was added a solution of 3.07 g (0.01 mole) trimethylphenylammonium p-toluenesulfonate in 8 ml alcohol. Sodium toluenesulfonate, which precipitated on cooling, was filtered off and washed with 4 ml alcohol. To the filtrate was added 2.98 g (0.01 mole) 6-(p-toluene-sulfonamido)-quinoline. The alcohol was evaporated, the temperature of the reaction mixture increased to 110°, and heating continued at 107-112° for 50 minutes, mixing the mass from time to time. After acidifica-tion with acetic acid, dimethyl aniline was removed by steam distillation. The residue was made alkaline with a concentrated solution of caustic, and the caustic solution combined with the oily product formed; it was crystallized by mixing with water and cooling. The water-washed precipitate was dissolved in 3% hydrochloric

acid, the solution boiled with carbon, filtered, and made alkaline. The 1.12 g of pinkish-white residue which formed was dissolved in ether in order to separate the small quantity of admixed starting materials, and the ether solution washed with dilute caustic. After vaporization of ether, the residue was crystallized from benzene and from a mixture of petroleum ether and benzene. White crystals, m.p. 121.5-122.5°, readily soluble in alcohol and benzene.

Found %: S 10.14, 10.20. $C_{17}H_{16}N_2O_2S$. Calculated %: S 10.26.

A brownish-pink precipitate of starting material was separated from the caustic solutions on acidification. After crystallization from alcohol, 1.22 g pinkish-white crystals were obtained, m.p. 195.5-197°. Consequently, yield of methylation product, based on 6-p-toluenesulfonamidoquinoline reacted, amounted to 60%.

6-(N-Methyl-p-toluenesulfonamido)-quinoline methyl iodide. 6-(N-Methyl-p-toluenesulfonamido)-quinoline was heated for 1 hour at 45° with an excess of methyl iodide; the excess of the latter was removed by distillation and the residue crystallized from a small volume of methyl alcohol. Very fine pale yellow needles, melting at 220-221° (with decomposition), readily soluble in hot water. The aqueous solution did not become yellow on addition of ammonia, nor did a precipitate form (in contrast with the methyl iodide of 6-p-toluenesulfonamidoquinoline).

Found %: I 27.72. $C_{18}H_{19}N_2O_2SI$. Calculated %: I 27.94.

N-Methylanilide of p-toluenesulfonic acid (prepared in collaboration with D. A. Krivosheya). 2.47 g (0.01 mole) of the anilide of p-toluenesulfonic acid, was methylated at 110° by the Rodionov procedure using trimethylphenylammonium hydroxide, which latter was prepared, as mentioned above, from 3.07 g (0.01 mole) trimethylphenylammonium p-toluenesulfonate. In order to free the compound obtained more completely from starting materials, it was dissolved in ether and washed with a caustic solution. Yield 1.80 g (70%). The product was twice crystallized from alcohol. M.p. 93.5-94.5° (according to the literature, m.p. is 94-95° [7-9]. On acidification of the caustic mother liquor, 0.2-0.4 g initial anilide of p-toluenesulfonic acid was separated.

Reaction between methyl-betaine 6-(p-toluenesulfonamido)-quinoline with methyl iodide. 0.5 g methyl-betaine 6-(p-toluenesulfonamido)-quinoline and 1.2 ml methyl iodide were heated in a sealed tube. The reaction took place very slowly at 60-65° – no change in color of reaction mixture occurred in a half-hour; above 70° the mixture's red color progressively turned yellow. At 75-80°, alkylation required 2.5 hours; at 105°, heating time was reduced to 40 minutes. The yellow crystalline precipitate was filtered, and washed repeatedly with dry benzene. Yield 0.71 g, i.e., almost theoretical. After two crystallizations from methanol, the compound formed pale yellow crystals (fine needles). The product was identical to the methyl iodide of 6-(N-methyl-p-toluenesulfonamido)-quinoline prepared from 6-(N-methyl-p-toluene-sulfonamido)-quinoline (m.p. 219-221°, mixed tests showed no depression).

Found %: I 27.92, 27.70. $C_{18}H_{19}O_2N_2SI$. Calculated %: I 27.94.

Reaction between methyl-betaine 6-(p-toluenesulfonamido)-quinoline and p-toluenesulfonic acid methyl ester. A mixture of 0.30 g methyl-betaine 6-(p-toluenesulfonamido)-quinoline and 0.30 g p-toluenesulfonic acid methyl ester was heated at 130-140° for 1.5 hours. Excess methyl ester was rinsed away with boiling benzene, the hygroscopic product was dissolved in a small volume of boiling water, and 1.5 g sodium iodide in 3 ml water added to the solution. The precipitate (0.40 g) crystallized from methanol as pale yellow needles. The product was the methyl iodide salt of 6-(N-methyl-p-toluenesulfonamido)-quinoline (m.p. 220-221°, no depression was observed in mixed melting point tests using the methyl iodide salts obtained by one of the above described procedures).

Reaction between methyl-betaine 6-(2',4'-dinitroanilino)-quinoline and methyl iodide [preparation of methyl iodide salt of 6-(N-methyl-2',4'-dinitroanilino)-quinoline]. 0.25 g methyl-betaine 6-(2',4'-dinitroanilino)-quinoline and 1 ml methyl iodide were heated for 1.5 hours in a sealed tube at 125-130°. A copious precipitate of orange crystals formed. Excess methyl iodide was evaporated, and the residue dissolved in 25 ml hot water. The solution was filtered and 1.5 g potassium iodide added, as a concentrated solution, to the filtrate. The precipitate which separated (0.30 g) was crystallized from methanol. Orange crystals with m.p. 204-205°.

Found %: I 26.82. $C_{17}H_{15}O_4N_4I$. Calculated %: I 27.22.

<u>Reaction between methyl-betaine 6-methoxy-8-(p-toluenesulfonamido)-quinoline and methyl iodide.</u>
0.40 g methyl-betaine 6-methoxy-8-(p-toluenesulfonamido)-quinoline and 1.5 g methyl iodide were heated in
a sealed tube at 100° for 1 hour. Yield 0.35 g. Bright yellow crystals (from methanol). Melting temperature
was in the 190.0-192.5° range, depending on rate of heating; a mixed melting point test with the methyl iodide
salt prepared from 6-methoxy-8-(N-methyl-p-toluenesulfonamido)-quinoline showed no depression.

Found %: I 26.22. $C_{18}H_{21}O_3N_2SI$. Calculated %: I 26.20.

<u>6-Methoxy-8-(N-methyl-p-toluenesulfonamido)-quinoline.</u> 0.80 g 6-methoxy-8-(p-toluenesulfonamido)-
quinoline was dissolved in 5 ml 8% potassium hydroxide and 35 ml water; to this solution 1.5 ml dimethyl
sulfate was added gradually with vigorous agitation together with enough caustic to maintain alkalinity. At
first the reaction mixture was cooled with ice, then the temperature was gradually increased to 15-20°. A
yellowish-white precipitate amounting to 0.68 g formed. After crystallization from benzine and from a mixture
of petroleum ether and benzene, the reaction product was a white crystalline material, m.p. 152.5-153°.

Found %: S 9.27. $C_{18}H_{18}O_3N_2S$. Calculated %: S 9.36.

The methyl iodide of 6-methoxy-8-(N-methyl-p-toluenesulfonamido)-quinoline was prepared in poor
yield by reaction of methyl iodide and 6-methoxy-8-(N-methyl-p-toluenesulfonamido)-quinoline at 120°. Better
results were obtained when 6-methoxy-8-(N-methyl-p-toluenesulfonamido)-quinoline was heated with excess
dimethyl sulfate at 100-105° for conversion into methyl-methosulfate and the latter, by reaction with potassium
iodide in aqueous solution transformed into the methyl iodide salt. Bright yellow crystals (from methanol),
m.p. about 190-192°.

<u>Methylchloride of 6-(N-benzoyl-p-toluenesulfonamido)-quinoline.</u> A mixture of 0.30 g methyl-betaine
6-(p-toluenesulfonamido)-quinoline and 0.20 g freshly distilled benzoyl chloride was heated on an oil bath at
120-130° for 1 hour. The prepared material was washed many times with absolute benzene. Yield 0.41 g
(90%). White crystals, very soluble in water, soluble in alcohol. Decomposition temperature approximately
215°. The compound was readily hydrolyzed with the splitting off of a benzoyl group: on addition of aqueous
ammonia solution to the material, a yellow color developed, and an orange crystalline precipitate of the
hydrate of methyl-betaine 6-(p-toluenesulfonamido)-quinoline rapidly separated.

Found %: S 7.09, 7.09. $C_{24}H_{21}N_2O_3SCl$. Calculated %: S 7.08.

SUMMARY

1. Dipolar ions, prepared when a proton is detached from the NH-group, readily react with alkyl
and acyl halides to form quaternary ammonium salts according to the scheme:
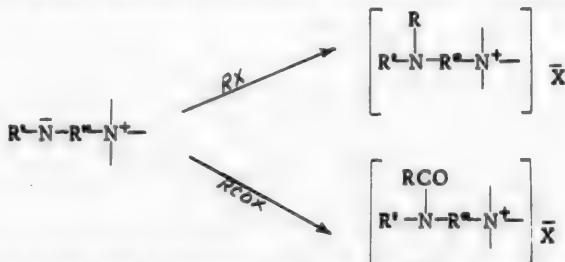
The ease of reaction is dependent on the nature of the groups attached to the negative N-atom.

2. Quaternary ammonium bases, proposed by V. M. Rodionov for alkylation of compounds containing
hydroxy groups, may also be used for alkylating the NH-group of aryl sulfonamides.

LITERATURE CITED

[1] A. M. Simonov, J. Gen. Chem. 10, 1220 (1940); 13, 51 (1943); 19, 2208 (1949); 20, 320 (1950);**
22, 1865 (1952); A. M. Simonov, N. P. Anshukova, J. Gen. Chem. 20, 1802 (1950).***

[2] E. Büllman, K. Jensen, H. Jensen, Bull. Soc. chim. (5), 1, 1661 (1934).

[3] A. Claus, E. Mohl, J. prak. Chem. (2), 54, 11 (1896); A. Claus, H. Howitz, J. prak. Chem. (2), 56,
438 (1897).

* See Consultants Bureau translation page 683

** See Consultants Bureau translation page 339

*** See Consultants Bureau translation page 1865

[4] V. M. Rodionov, Bull. Soc. chim (4) 39, 305 (1926); 45, 109 (1929).

[5] W. H. Mills, J. G. Brekenridge, J. Chem. Soc. 1932, 2213.

[6] R. Huisgen, Ann. 559, 182 (1948).

[7] R. Otto. J. prak. Chem. (2) 47, 371 (1893).

[8] W. Michler, K. Meyer, Ber. 12, 1793 (1879).

[9] F. Arndt, C. Martius, Ann. 499, 265 (1932).

STUDIES ON AMINOACIDS

II. CATALYTIC REDUCTION OF ESTERS OF OXIMIDO-(ISONITROSO)-CARBOXYLIC ACIDS

S. I. Lurye, G. A. Ravdel, and E. S. Chaman

Carbonyl and oximido groups may be reduced [1] to hydroxy or amino groups, respectively, by hydrogen in presence of various catalysts, with the oximido group being more readily reduced than the carbonyl group [2]. For reduction in acid solution, palladium or platinum are used as catalysts; in neutral solution — pyrophoric nickel or other metals.

The present paper is devoted to catalytic reduction reaction studies on both the ethyl ester of isonitrosoaceto-acetic acid and the diethyl ester of isonitrosomalonic acid using Raney nickel.

$$CH_3\text{--}\underset{\underset{O}{\|}}{C}\text{--}\underset{\underset{N\text{--}OH}{\|}}{C}\text{--}COOC_2H_5 \xrightarrow{3H_2} CH_3\text{--}\underset{\underset{OH}{|}}{CH}\text{--}\underset{\underset{NH_2}{|}}{CH}\text{--}COOC_2H_5$$

In as much as isonitrosoacetoacetic ester contains both carbonyl and oximido groups in its molecule, it was quite natural to hope to study the reduction of both of these groups together at one stage. To this end, tests were made and we found it was possible, in neutral medium, to reduce both the oximido and the carbonyl groups at the same time by performing the reaction at 300 atm. and 15-20 minutes. α-Amino-β-hydroxybutyric acid was obtained with 30-37% yield. Under milder conditions, instead of α-amino-β-hydroxybutyric acid, the corresponding pyrazine was obtained [4], this proves that only the oximido group was reduced and that the molecules of the aminoacetoacetic ester which formed interact with one another. The severe conditions required for reduction of isonitrosoacetoacetic ester to α-amino-β-hydroxybutyric acid in neutral solution, together with poor yield, compelled us to search for other procedures for preparation of α-amino-β-hydroxybutyric acid. Best results were obtained by two-stage reduction of isonitrosoacetoacetic ester [5]:

$$CH_3C\text{--}\underset{\underset{O}{\|}}{C}\text{--}\underset{\underset{N\text{--}OH}{\|}}{C}\text{--}COOC_2H_5 \xrightarrow[(CH_3CO)_2O]{2H_2} CH_3\text{--}\underset{\underset{O}{\|}}{C}\text{--}\underset{\underset{NHCOCH_3}{|}}{CH}\text{--}COOC_2H_5 \xrightarrow{H_2} CH_3CH\text{--}\underset{\underset{OH}{|}}{}\underset{\underset{NHCOCH_3}{|}}{CH}\text{--}COOC_2H_5 \longrightarrow CH_3\text{--}\underset{\underset{OH}{|}}{CH}\text{--}\underset{\underset{NH_2}{|}}{CH}\text{--}COOH$$
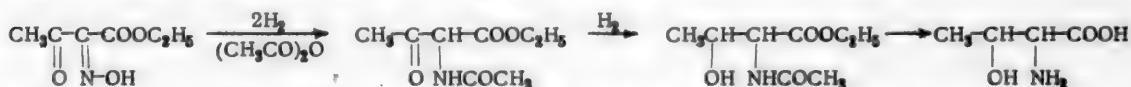
it was first reduced to N-acetamido-acetoacetic ester using zinc in an acetic acid solution or using hydrogen in a mixture of acetic acid and acetic anhydride in presence of palladium [6]; the N-acetamidoacetoacetic ester was then reduced in neutral medium using pyrophoric nickel to form the ethyl ester of N-acetamido-β-hydroxybutyric acid, which on saponification was transformed into α-amino-β-hydroxybutyric acid. Overall yield of α-amino-β-hydroxybutyric acid was 60-65% of theoretical.

Our experimental studies on reduction of carbonyl and oximido groups showed that isonitrosoacetoacetic ester could be directly reduced using Raney nickel to the ester of N-acetamido-β-hydroxybutyric acid in one stage, however certain necessary conditions must be maintained. In the first place, an acetylating agent must be present in the reaction mixture to react with the newly formed amino group, and in the second place, the pH of the mixture must be 4 5-5; this is very important for maintaining catalytic activity of pyrophoric nickel. These conditions may be provided by using acetic anhydride as the reaction medium.

By reducing isonitrosoacetoacetic ester with hydrogen in acetic anhydride medium with Raney nickel, we were able to prepare α-amino-β-hydroxybutyric acid in a 62% yield. When the oximido group is reduced to an amino group, a molecule of water is formed which produces two moles of acetic acid from acetic anhydride. In addition, a mole of acetic acid is formed in acetylating the amino group. Accumulation of three moles of acetic acid changes the pH of the medium, and this interferes with the normal course of the reduction process. Sodium acetate was added to minimize the effect of acetic acid on the reaction. Under these conditions, α-amino-β-hydroxybutyric acid was obtained with a 72% yield rather than a 62% yield. Contrariwise, by addition of a known excess of acetic acid, the yield of α-amino-β-hydroxybutyric acid was considerably reduced, at least from the increased quantity of acid added.

We noticed that absorption of hydrogen does not proceed uniformly in reduction of isonitrosoacetoacetic ester. The first two moles of hydrogen are absorbed rapidly at 25-60°; the third mole is absorbed slowly at 90-95°. This phenomenon, wholly concordant with the known facts about the differing reduction behavior of carbonyl and oximido groups, is indicative of the two-stage character of the reduction process. In order to ascertain the reduction conditions in both of these stages separately, we carried out the process of preparing a-amino-β-hydroxy-butyric acid in two steps in an acetic anhydride medium using the identical catalyst (Raney nickel). Reduction of isonitrosoacetoacetic ester at 20-25° led to formation of N-acetamidoacetoacetic ester with a 82-83% yield. The latter was reduced at 90-95°, although the reaction proceeded slowly. The resulting ethyl ester of N-acetamido-β-hydroxybutyric acid was saponified, and a-amino-β-hydroxybutyric acid separated with a yield 75.5% of theoretical. We were thus able to show that oximido and carbonyl groups could be reduced in a medium of acetic anhydride using Raney nickel, during which both groups could be reduced separately or both at once.

In addition to reduction of the ester of isonitrosoacetoacetic acid, we investigated reduction of the diethyl ester of isonitrosomalonic acid in an acetic anhydride medium. This compound is usually reduced using zinc dust in acetic acid [7] or by hydrogen in alcoholic medium in the presence of Raney nickel or palladium [8]. In both of these conditions, the diethyl ester of aminomalonic acid becomes acetylated. Under our conditions reduction directly gives the diethyl ester of N-acetamidomalonic acid with a yield 89-90% of theoretical.

We extend thanks to E. M. Elina, S. A. Fuks, E. A. Ignatyeva, and V. V. Ogurtsova for performing the analyses.

EXPERIMENTAL

The ethyl ester of isonitroso-(oximido)-acetoacetic acid was prepared by the Adkins method [3]. Yield, after crystallization of product from toluene, was 73-75% of theoretical. M.p. 58-59°. Diethyl ester of isonitroso-(oximido)-malonic acid was prepared according to a patent [7].

1. Reduction of isonitrosoacetoacetic acid ethyl ester. 31.8 g ethyl ester of isonitrosoacetoacetic acid, 4.5 g freshly fused sodium acetate, 5 g pyrophoric Raney nickel, and 60 ml acetic anhydride were reduced in an autoclave, with agitation, at an initial pressure of 68-70 atm. The reaction was initiated at 15-20° and the temperature gradually brought to 55° in 1-1.5 hours, during this time 12-14 liters of hydrogen were absorbed. Subsequent absorption of the last 4-6 liters of hydrogen took place slowly in 3-4 hours at 95-97°. At the end of hydrogen absorption, the autoclave was cooled and the reaction mixture dumped and filtered; the catalyst was washed with alcohol, the washings added to the main filtrate and evaporated to dryness under vacuum. The residue was then boiled with 100 ml conc. hydrochloric acid for 4 hours, it was boiled with carbon for the last 0.5 hour. The hot solution was filtered and evaporated under vacuum; after vaporization of the acid, the residue was twice taken up with water and evaporated to dryness under vacuum. The dry residue was extracted with 120 ml hot alcohol and diethylamine or aniline added in small portions to the still warm filtered solution until neutral to bromothymol-blue. It was allowed to stand and was filtered the next day. The crude a-amino-β-hydroxybutyric acid was dissolved in 2.5 times its volume of water and precipitated by four volumes of alcohol (based on the water). Yield 72%. M.p. 228-229°. The a-amino-β-hydroxybutyric acid prepared by this procedure contained 21% threonine and 79% allothreonine (microbiological analysis).

Found %: C 40.39; H 7.54; N 11.94. $C_4H_9O_3^!N$. Calculated %: C 40.31; H 7.62; N 11.76.

Reduction of isonitrosoacetoacetic ester without sodium acetate gave a-amino-β-hydroxybutyric acid with a yield 62% of theoretical.

2. Preparation of N-acetamidoacetoacetic acid ethyl ester. 31.8 g isonitrosoacetoacetic acid ethyl ester, 60 ml acetic anhydride, and 5 g Raney nickel were reduced with hydrogen in an autoclave at 21-25° with an initial pressure of 55-60 atm. The required quantity of hydrogen was absorbed in 4 hours. Reaction mass was removed from the autoclave and filtered. The catalyst was washed on the filter with water. Filtrate was diluted with 250 ml water and extracted several times with chloroform. The chloroform extracts were combined, washed twice with small quantities of water, dried and distilled. The oily residue was dried under vacuum at 60-80° (bath temperature). On cooling, the entire mass crystallized. It was triturated with a small amount of petroleum ether and pressed out on a funnel; melting point of the ethyl ester of N-acetamidoacetoacetic acid was 43-45°. A test mixture with the ethyl ester of N-acetamidoacetoacetic acid prepared by reduction with zinc , melted without depression. Yield 82.8% of theoretical.

3. Reduction of N-acetamidoacetoacetic acid ethyl ester. 37.4 g N-acetamidoacetoacetic acid ethyl ester, 60 ml acetic anhydride, 4.5 g freshly fused sodium acetate, and 5 g Raney nickel were charged into an autoclave and reduced with hydrogen using an initial pressure of 77 atm. Temperature slowly increased to

85-90°, and at this temperature the necessary quantity of hydrogen was absorbed in a 7-8 hour period. At the end of the reaction, the mass was dumped, filtered, and the catalyst washed with 100-120 ml of alcohol. The alcohol washings were combined with the main filtrate and the whole taken to dryness under vacuum. The residue was treated with 100 ml conc. hydrochloric acid and boiled for 4 hours for the last 0.5 hour with activated carbon. It was filtered and the filtrate evaporated to dryness under vacuum; it was twice more taken up with water and evaporated to dryness each time. The residue was then dissolved in 100 ml boiling alcohol, the solution filtered, the sodium chloride residue on the filter was washed with 30 ml alcohol and the washing added to the main filtrate, and to the still warm alcohol solution diethylamine or aniline was gradually added (bromothymol-blue indicator). The mixture was permitted to stand for 20 hours, filtered, and the residue washed with alcohol and dried. For purification it was dissolved in twice its volume of water and precipitated by 4 times this quantity of alcohol. The melting point of a-amino-β-hydroxybutyric acid was 228-229°. Yield 75.5% of theoretical.

Found %: C 40.12; H 7.60; N 11.62. $C_4H_9O_3N$. Calculated %: C 40.31; H 7.62, N 11.76.

4. Reduction of N-acetamidoacetoacetic ester under the conditions of Experiment 3 but without sodium acetate gave a-amino-β-hydroxybutyric acid with a yield 62% of theoretical.

5. Reduction of N-acetamidoacetoacetic ester in presence of acetic acid. The reaction was run under conditions of Experiment 3, but 34.3 ml acetic acid was used in place of sodium acetate. Yield of a-amino-β-hydroxybutyric acid was 34.4%. Yield of a-amino-β-hydroxybutyric acid was reduced to 24% of theoretical by addition of 60 ml glacial acetic acid.

6. Diethyl ester of N-acetamidomalonic acid. 105.75 g diethyl ester of isonitrosomalonic acid, 170 ml acetic anhydride, and 15 g Raney nickel were charged into an autoclave and reduced with an initial pressure of 70-80 atm. at 19°; the temperature gradually increased to 73°. The reduction reaction took place in 1-1.5 hours. Quantity of hydrogen absorbed was somewhat greater than theoretical. The autoclave was gradually cooled and the reaction mass removed and filtered. The catalyst was repeatedly washed with alcohol and then with water. The main filtrate, the alcoholic washings, the alcohol with which the autoclave was rinsed, and the water washings were all combined and evaporated to dryness under vacuum. The residue was carefully triturated with carbon tetrachloride and filtered. It was washed once on the filter with carbon tetrachloride. We obtained 109 g diethyl ester of N-acetamido-malonic acid (5 g of this were separated from the carbon tetrachloride), i.e., 89.7% of theoretical. M.p. 94-96°.

Found %: C 49.72; H 6.79; N 6.48. $C_9H_{15}O_5N$. Calculated %: C 49.74; H 6.96; N 6.45.

SUMMARY

It was shown that esters of isonitroso-(oximido)-carboxylic and ketocarboxylic acids can be reduced to the corresponding N-acetamidocarboxylic and N-acetamidohydroxycarboxylic esters using hydrogen with Raney nickel in an acetic anhydride medium.

LITERATURE CITED

[1] W. Hartung, L. C. Munch, J. Am. Chem. Soc., 51, 2262 (1929); K. L. Waters, W. Hartung, J. Org. Chem. 10, 524 (1945).

[2] S. L. Lelchuk and others, Prog. Chem. 14, 185 (1945).

[3] H. Adkins, S. W. Reeve, J. Am. Chem. Soc. 60, 1328 (1938)

[4] C. F. Winaus, H. Adkins, J. Am. Chem. Soc. 55, 4169 (1933).

[5] K. Pfister, C. Robinson, J. Am. Chem. Soc. 71, 1101 (1949).

[6] N. F. Albertson, B. F. Tullar, J. A. King, B. B. Fishburn, S. Archer, J. Am. Chem. Soc. 70, 1150 (1948).

[7] U.S. Pat. 583307 (1946).

[8] C. E. Redemann, M. S. Dunn, J. Biol. Chem. 130, 341 (1939); H. K. Snyder, S. W. Smith, J. Am. Chem. Soc. 66, 350 (1944).
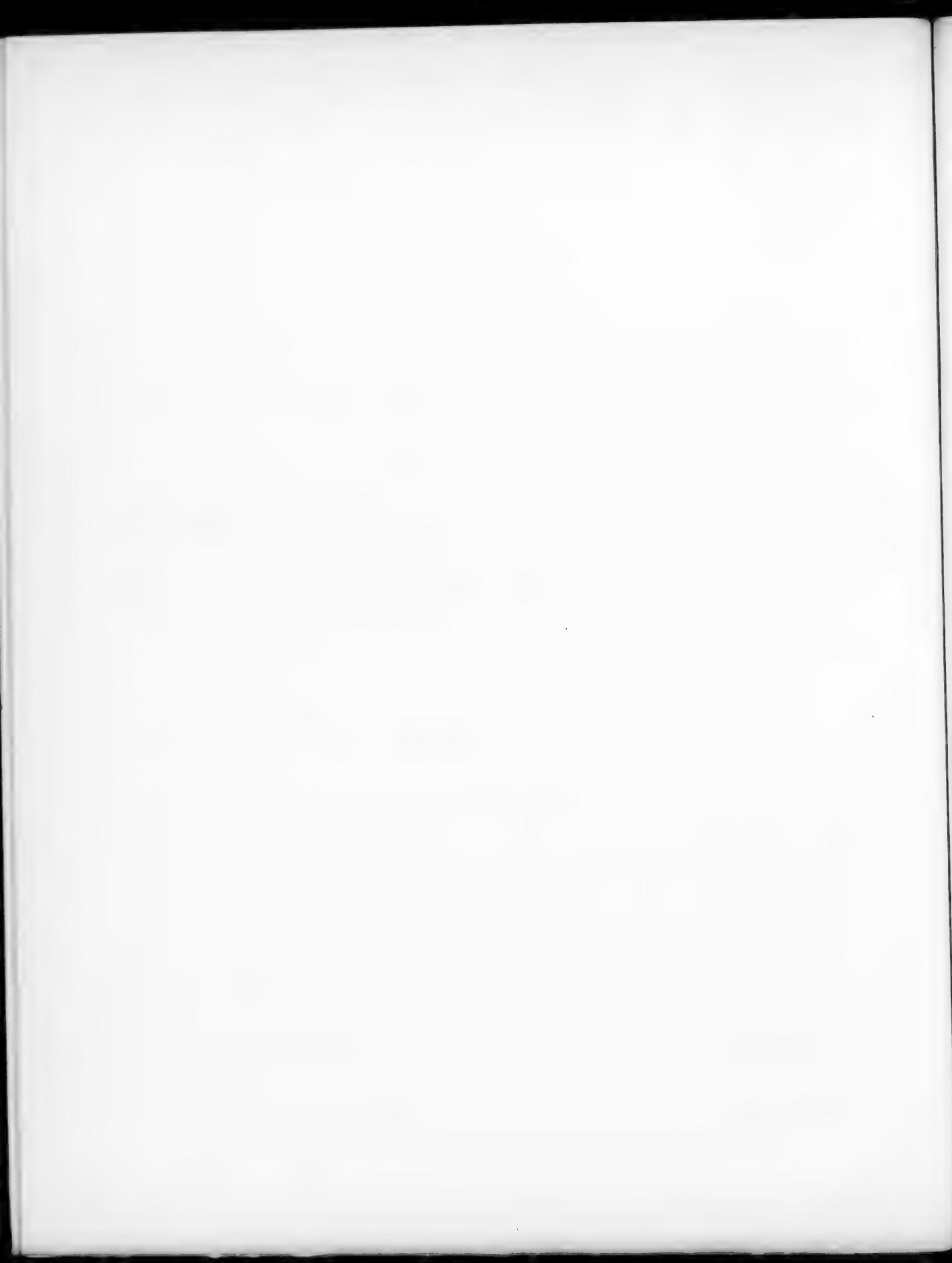
SYNTHESIS OF SEVERAL DERIVATIVES OF PARAAMINOSALICYLIC ACID

E. S. Golombik and M. N. Shchukina

p-Aminosalicylic acid has acquired great interest at present as an anti-tubercular drug. However, it has an inherent shortcoming – the property of rapid elimination from the organism, in consequence of which large doses, aggregating 18-20 g per day and up to 1 kg per course of therapy, are used for medical treatment of tubercular patients. The development of compounds having the same therapeutic activity as p-aminosalicylic acid but which would be more slowly eliminated from the organism is very important. It was natural to suppose these requirements could be satisfactorily met by using certain derivatives of p-aminosalicylic acid, among which it was fully probable that substances could be found having suitable therapeutic behavior with respect to hydrolysis and other physico-chemical properties and which would be more slowly eliminated from the organism.

According to available literature [1,2] a number of p-aminosalicylic acid derivatives showed anti-tubercular activity in vitro; those derivatives which could readily hydrolyze to it showed activity most similar to p-aminosalicylic acid. However, none of the compounds of this type exceeded p-aminosalicylic acid with regard to activity in vitro [2]. Based on this, the question was raised as to whether bacteriostatic activity of derivatives of p-aminosalicylic acid was dependent on their hydrolysis in the organism. Data [3] published in the past year on the high tubercularstatic activity of p-aminosalicylic acid phenyl ester, both in tests in vitro and in experiments on mice, led us to conclude that the activity of this and possibly other derivatives of p-aminosalicylic acid was manifested by the substance as a whole and not by its hydrolysis product – p-aminosalicylic acid.

In the present paper we describe the preparation and chemical properties of: several N-acyl derivatives of p-aminosalicylic acid and their esters; N-carbalkoxy substituted p-aminosalicylic acids and their esters; [bis-(4-carbethoxy-3-hydroxyphenylamino)]-methane (I); and [bis-(4-carbethoxy-3-hydroxyphenyl)]-urea (II).
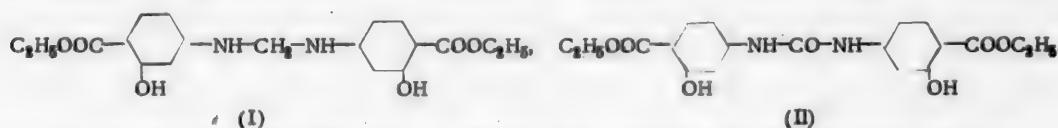
As a starting material for preparation of derivatives of p-aminosalicylic acid we preferred to use its esters, because the acid is unstable and readily splits out carbon dioxide, particularly in acid media, and in many cases readily becomes tarry.

A convenient method for preparation of p-aminosalicylic acid esters is catalytic reduction, in presence of skeletal nickel catalyst, of the corresponding ester of p-nitrosalicylic acid, esterification of which latter is readily performed using alcohol in presence of sulfuric acid [4]. Esters of p-aminosalicylic acid may also be prepared directly by esterification of the acid with alcohol in presence of excess sulfuric acid [5]. The phenyl ester of p-aminosalicylic acid, the synthesis of which has not been published, was prepared by us by reduction, in presence of skeletal nickel catalyst, of the phenyl ester of p-nitrosalicylic acid. This latter was synthesized by two methods: 1) by action of phosphorous oxychloride on a melt of equimolar quantities of p-nitrosalicylic acid and phenol with subsequent heating of the mixture at 120-130°; 2) boiling in a xylene solution a mixture of equimolar quantities of p-nitrosalicylic acid and phenol in presence of phosphorous pentachloride [6]. The first method was the more suitable, and we were able to prepare the final product with a yield about 57% of theoretical

The N-acyl derivatives were prepared by usual methods – by action of acid chlorides on a solution of p-aminosalicylic acid in pyridine. The methylene-bis-ethyl ester was synthesized by condensation of p-amino-salicylic acid ethyl ester with formalin in an alcoholic medium. Attempts to prepare methylene-bis-p-amino-salicylic acid by condensation of p-aminosalicylic acid with formalin or by saponification of its methylene-bis-ethyl ester led to formation of colored substances, which did not melt on heating to 350°, were readily decarboxylated, and could not be purified. Analytical data on these substances does not permit us to judge their structure.

[Bis-(4-carbethoxy-3-hydroxyphenyl)]-urea was prepared by two methods: 1) condensation of p-amino-salicylic acid ethyl ester with urea at 140-160°; yield about 36% of theoretical [7]; 2) by reaction of phosgene with p-aminosalicylic acid ethyl ester dissolved in boiling benzene or chloroform; yield 93% of theoretical. Reaction temperature was quite important here — only the hydrochloric acid salt of p-aminosalicylic acid ethyl ester was separated when heating was at 40-50°.

The urethanes of p-aminosalicylic acid and its esters were prepared by reaction with the corresponding chlorocarbonic esters. It was most satisfactory to carry out this reaction in a benzene solution in presence of dimethylaniline. Under this condition almost pure materials were prepared in large yield, approaching in some cases 99% of theoretical. Performing this reaction in an alcoholic solution in presence of sodium ethylate [8] led to separation of the corresponding urethane with a yield which did not exceed 50% of theoretical.

EXPERIMENTAL

1. N-Hendecenoyl-p-aminosalicylic acid. To a solution of 3 g p-aminosalicylic acid in 30 ml dry pyridine we added 4 g hendecenoyl chloride dropwise with cooling. The solution obtained was then heated for 3 hours at 40-50°. After evaporation of the pyridine in vacuum, the residue was poured into water; in order to remove unreacted acid chloride the water solution was extracted with ether and treated with acetic acid until acid to litmus. The separated oil was extracted with ether, washed with water and dried over calcined sodium sulfate. The solvent was removed, and the residue which was an oily readily crystallizable material purified by recrystallization from ethyl acetate.

We obtained 6 g (96% of theory) N-hendecenoyl-p-aminosalicylic acid in the form of colorless platelets; m.p. 176° with decomposition; readily soluble in alcohol, ether, acetone, and benzene; insoluble in petroleum ether and water. It gave a violet color with ferric chloride in alcohol solution.

3.839 mg substance: 9.485 mg CO_2; 2.690 mg H_2O. 3.591 mg substance: 8.890 mg CO_2; 2.500 mg H_2O. 7.045 mg substance: 0.280 ml N_2 (20°, 737 mm). Found %: C 67.38, 67.52; H 7.84, 7.79; N 4.49. $C_{18}H_{25}O_4N$. Calculated %: C 67.71; H 7.85; N 4.39.

2. N-Hendecanoyl-p-aminosalicylic acid was prepared in the same manner as N-hendecenoyl-p-amino-salicylic acid. The yield was 10 g (95.3% of theoretical) from 5 g p-aminosalicylic acid. Colorless crystals, m.p. 183-184° with decomposition, readily soluble in alcohol, acetone, and chloroform; less soluble in benzene and ether; and insoluble in water. It gave a violet color with ferric chloride in alcoholic solution.

3.868 mg substance: 9.513 mg CO_2; 2.884 mg H_2O. 8.300 mg substance: 0.335 ml N_2 (21.5°, 718 mm). Found %: C 67.07; H 8.34; N 4.42. $C_{18}H_{27}O_4N$. Calculated %: C 67.29; H 8.41; N 4.36.

3. Isoamyl ester of p-nitrosalicylic acid. A solution of 25 g p-nitrosalicylic acid and 10 ml concentrated sulfuric acid in 200 ml dry isoamyl alcohol was boiled for 24 hours. After evaporating excess alcohol under vacuum, the residue was poured into water. The dark-colored oil which separated was extracted with ether, washed with water and with a saturated solution of sodium bicarbonate, dried over calcined sodium sulfate, and distilled. 22 g yield (63.7% of theoretical). Thick, pale yellow liquid, b.p. 155° at 0.6 mm, readily soluble in most organic solvents, insoluble in water.

4. Isoamyl ester of p-aminosalicylic acid.• A solution of 22 g p-nitrosalicylic acid isoamyl ester in 200 ml alcohol was agitated in a hydrogen atmosphere in presence of 2 g nickel catalyst paste at 50-60° and 15 atm. The calculated quantity of hydrogen was absorbed in 30-45 minutes. After cooling, the solution was filtered and concentrated under vacuum, and the residue poured into water. The almost colorless crystals which formed were separated and recrystallized from 50% aqueous alcohol. Yield 15 g, which corresponds to 77.5% of theoretical. The substance formed colorless rhombic flakes, m.p. 79-80°, readily soluble in most organic solvents.

3.682 mg substance: 8.738 mg CO_2; 2.408 mg H_2O. 6.890 mg substance: 0.389 ml N_2 (21.5°, 732 mm). Found %: C 64.72; H 7.32; N 6.30. $C_{12}H_{17}O_3N$. Calculated %: C 64.57; H 7.62; N 6.28.

5. Phenyl ester of p-nitrosalicylic acid. a) A suspension of 9.2 g p-nitrosalicylic acid (1 mole), 4.7 g phenol (1 mole) and 3.7 g phosphorous pentachloride (0.35 mole) in 100 ml absolute xylene was heated at 90° for 30 minutes, and then for 1.5-2 hours at 120-130° until liberation of hydrogen chloride ended. The reaction

_____
• Using this method, we prepared the ethyl, isopropyl, and isobutyl esters of p-aminosalicylic acid.

mixture remained homogeneous during heating. At the end of the reaction, xylene was vaporized under vacuum, and the oily residue treated with a saturated aqueous solution of sodium bicarbonate. The crystals were separated, dried, and recrystallized from acetic acid. From the sodium bicarbonate solution we recovered 3 g p-nitrosalicylic acid. The yield of p-nitrosalicylic acid phenyl ester was 3.5 g (39.8% of theoretical). Pale yellow crystals, m.p. 148-149°; readily soluble in chloroform, acetone, ethyl acetate, and dioxane; poorly soluble in alcohol and ether; insoluble in water and bicarbonate solution. It gave a violet color with ferric chloride in acetone solution.

5.049 mg substance: 11.151 mg CO_2; 1.632 mg H_2O. 7.215 mg substance: 0.342 ml N_2 (26°, 738.3 mm). Found %: C 60.23; H 3.62; N 5.29. $C_{13}H_9O_5N$. Calculated %: C 60.23; H 3.48; N 5.41.

b) A carefully ground mixture of 2 g p-nitrosalicylic acid (1 mole) and 1 g phenol (1 mole) was melted at 140°. The melt was cooled to 100° and 0.8 g (about 0.5 mole) phosphorous oxychloride added; the mixture was then heated at 120-130° for 2-3 hours until evolution of hydrogen chloride ceased. The mixture remained liquid during heating. After cooling, the dark-colored melt was triturated with water and heated to 50° with a solution of sodium bicarbonate; the precipitate which formed was filtered and recrystallized from acetic acid. We obtained 1.6 g (56.5% of theoretical) p-nitrosalicylic acid phenyl ester, m.p. 148-149°.

6. Reduction of p-nitrosalicylic acid phenyl ester. A solution of 3 g p-nitrosalicylic acid phenyl ester in 50 ml ethyl acetate was agitated in a hydrogen atmosphere in presence of 0.3 g skeletal nickel catalyst at 50-60° and 20 atm. After 30 minutes the calculated quantity of hydrogen had been absorbed. After removal of catalyst, the solution was decolorized with carbon and sodium hydrosulfite, the solvent evaporated under vacuum, and the residue crystallized from ethyl alcohol. Yield of p-aminosalicylic acid phenyl ester was 1.85 g (69.8% of theoretical). Colorless needles, m.p. 147-148.5°, readily soluble in most organic solvents and insoluble in water. A mixed test with the initial p-nitrosalicylic acid phenyl ester melted at 115°.

3.218 mg substance: 8.089 mg CO_2; 1.471 mg H_2O. 7.815 mg substance: 0.423 ml N_2 (20°, 741.2 mm). Found %: C 68.55; H 5.11; N 6.24. $C_{13}H_{11}O_3N$. Calculated %: C 68.12; H 4.80; N 6.11.

7. [Bis-(4-carbethoxy-3-hydroxyphenyl)]-methane. We added 5 ml 36.2% aqueous formalin solution, with stirring, to a solution of 3 g p-aminosalicylic acid ethyl ester (m.p. 115°) in 15 ml ethyl alcohol heated at 50°. In several minutes a colorless precipitate formed, which was separated, washed with small portions of alcohol, and dried in a vacuum dessicator. Yield 2.8 g (90.3% of theoretical). Colorless crystals, m.p. 180-182°; readily soluble in benzene, ether, and acetone; poorly soluble in ethyl acetate, chloroform, and alcohol; and insoluble in water. It crystallized from dioxane, but its melting point then fell to 164°. Consequently the prepared material was analyzed without adequate purification. It gave a color reaction with ferric chloride.

3.701 mg substance: 8.273 mg CO_2; 1.919 mg H_2O. 6.775 mg substance: 0.471 ml N_2 (27.5°, 725 mm). Found %: C 60.96; H 5.80; N 7.52. $C_{19}H_{22}O_6N_2$. Calculated %: C 60.96; H 5.88; N 7.49.

8. [Bis-(4-carbethoxy-3-hydroxyphenyl)]-urea. a) A mixture of 1.8 g p-aminosalicylic acid ethyl ester (2 moles) and 0.3 g urea (1 mole) was heated at 140-160° for a period of 10 hours until evolution of ammonia ceased. After cooling the colored melt was ground up with alcohol. The separated precipitate, after repeated recrystallization from alcohol using activated carbon, formed colorless needles m.p. 215-216°. Yield 0.7 g (36.2% of theoretical); the substance was readily soluble in dioxane and acetone, poorly soluble in benzene, chloroform, ethyl acetate, and ether. A positive test was obtained for the phenolic hydroxyl group using ferric chloride.

3.494 mg substance: 7.530 mg CO_2; 1.610 mg H_2O. 8.305 mg substance: 0.574 ml N_2 (25.5°, 720 mm). Found %: C 58.77; H 5.15; N 7.58. $C_{19}H_{20}O_7N_2$. Calculated %: C 58.76; H 5.15; N 7.22.

b) To a solution of 1.8 g p-aminosalicylic acid ethyl ester in 20 ml absolute benzene (or chloroform) we added 4 ml of a 25% solution of phosgene in absolute benzene. A precipitate formed immediately. The reaction mixture was boiled for 2 hours; on cooling the residue was separated, washed with ether and recrystallized from alcohol. We obtained 1.8 g [bis-(4-carbethoxy-3-hydroxyphenyl)]-urea in the form of colorless needles melting at 215°. A mixed melting point test with a sample of material prepared in the previous experiment showed no depression. Yield was 93.2% of theoretical.

9. N-Carbethoxy-p-aminosalicylic acid. To a vigorously agitated suspension of 3 g p-aminosalicylic acid in 20 ml absolute alcohol at 10-15°, we added 2.2 g ethyl chlorocarbonate and a solution of sodium ethylate (1.5 g sodium in 40 ml absolute alcohol). The reaction mixture was then heated for 1 hour at 40-50° and diluted with water on cooling. The aqueous solution was neutralized with 10% hydrochloric acid. The precipitate was separated

and recrystallized from 50% aqueous alcohol with use of activated carbon. Yield 2.2 g (50% of theoretical). The substance formed colorless needles, m.p. 210°; readily soluble in alcohols, ether, ethyl acetate, and acetone; less soluble in benzene and petroleum ether; and insoluble in water. In alcohol solution it gave a violet color with ferric chloride.

3.594 mg substance: 7.044 mg CO_2; 1.619 mg H_2O. 8.700 mg substance: 0.500 ml N_2 (23°, 733 mm). Found %: C 53.45; H 5.04; N 6.39. $C_{10}H_{11}O_5N$. Calculated %: C 53.34; H 4.89; N 6.22.

10. N-Carbethoxy-p-aminosalicylic acid ethyl ester. a) To a solution of 3.6 g (1 mole) p-aminosalicylic acid ethyl ester in 40 ml absolute ethyl alcohol, agitated and cooled to 5°, we gradually added 2.2 g (1 mole) ethyl chlorocarbonate and a solution of sodium alcoholate (0.7 g sodium in 30 ml absolute alcohol). The latter was added at such a rate that the temperature did not exceed 15°. The reaction mass was then stirred for 2 hours at room temperature, sodium chloride separated, excess alcohol evaporated under vacuum, and the residue recrystallized from alcohol. The ethyl ester of N-carbethoxy-p-aminosalicylic acid was prepared in the form of colorless prisms, m.p. 149-151°; readily soluble in acetone and ethyl acetate, moderately soluble in alcohols, less soluble in benzene and ether, and insoluble in water. Yield 1.7 g, corresponds to 33.8% of theoretical. A positive test was obtained for the phenolic hydroxyl group using ferric chloride.

3.648 mg substance: 7.644 mg CO_2; 1.908 mg H_2O. 6.845 mg substance: 0.344 ml N_2 (23°, 727 mm). Found %: C 56.59; H 5.79; N 5.54. $C_{12}H_{15}O_5N$. Calculated %: C 56.92; H 5.93; N 5.53.

11. N-Carbethoxy-p-aminosalicylic acid isobutyl ester was prepared in the same way as N-carbethoxy-p-aminosalicylic acid ethyl ester. Because the substance was soluble in benzene, it was separated in the following manner: the reaction mixture was treated with a 5% hydrochloric acid solution for removal of excess dimethyl aniline, washed with water, and dried over calcined sodium sulfate. The residue after removal of solvent was recrystallized from ethyl alcohol. From 1.1 g p-aminosalicylic acid isobutyl ester we obtained 1.4 g (94.5% of theoretical) N-carbethoxy-p-aminosalicylic acid isobutyl ester as colorless octahedral needles, m.p. 132-134° (from alcohol); readily soluble in most organic solvents, insoluble in water; it gave a color reaction with ferric chloride in alcoholic solution.

4.618 mg substance: 10.099 mg CO_2; 2.839 mg H_2O. Found %: C 59.64; H 6.87. $C_{14}H_{19}O_5N$. Calculated %: C 59.79; H 6.76.

12. N-Carbethoxy-p-aminosalicylic acid isopropyl ester was prepared similarly to the foregoing. Yield 1.3 g, which corresponds to 94.8% of theoretical. The substance formed colorless pyramids, m.p. 143-145° (from alcohol); readily soluble in acetone, benzene, and alcohol; insoluble in ether, petroleum ether, and water; it gave an intense violet color with ferric chloride.

3.540 mg substance: 7.598 mg CO_2; 2.089 mg H_2O. Found %: C 58.54; H 6.60. $C_{13}H_{17}O_5N$. Calculated %: C 58.43; H 6.37.

13. The isobutyl ester of N-carbisobutoxy-p-aminosalicylic acid was prepared in the same way as was the previous ester. Yield 77.5% of theoretical. Colorless rhombic flakes (from hexane), m.p. 65-67°; readily soluble in most organic solvents and insoluble in water; it gave an intense violet color with ferric chloride.

4.268 mg substance: 9.770 mg CO_2; 2.968 mg H_2O. Found %: C 62.43; H 7.78. $C_{16}H_{23}O_5N$. Calculated %: C 62.14; H 7.44.

14. The isobutyl ester of N-carbisopropoxy-p-aminosalicylic acid was prepared in the same manner as the previous esters with a yield 95% of theoretical. It formed cubic prisms (from petroleum ether, 45-65° fraction), m.p. 72-74°; readily soluble in most organic solvents, insoluble in water.

3.928 mg substance: 8.770 mg CO_2; 2.530 mg H_2O. Found %: C 60.89; H 7.21. $C_{15}H_{21}O_5N$. Calculated %: C 61.02; H 7.12.

15. The isopropyl ester of N-carbisopropoxy-p-aminosalicylic acid was prepared in the same manner. Yield 1.40 g, corresponding to 97.1% of theoretical. Colorless cubic prisms with m.p. 90-92° (from hexane); readily soluble in most organic solvents and insoluble in water.

4.580 mg substance: 10.068 mg CO_2; 2.767 mg H_2O. Found %: C 59.95; H 6.76. $C_{14}H_{19}O_5N$. Calculated %: C 59.79; H 6.76.

16. The isopropyl ester of N-carbisobutoxy-p-aminosalicylic acid was prepared in the very same way as the previous ester. The yield was 99% of theoretical. Colorless flakes with m.p. 77-79° (from hexane); readily soluble in most organic solvents and insoluble in water.

3.690 mg substance: 8.302 mg CO_2; 2.400 mg H_2O. Found %: C 61.36; H 7.28. $C_{15}H_{21}O_5N$. Calculated %: C 61.02; H 7.12.

SUMMARY

A series of derivatives of p-aminosalicylic has been synthesized namely: its esters, N-carbalkoxy-p-aminosalicylic acids and their esters, N-acyl-p-aminosalicylic acids, [bis-(4-carbethoxy-3-hydroxyphenyl)]-urea, and [bis-(4-carbethoxy-3-hydroxyphenylamino)]-methane.

LITERATURE CITED

[1] H. Erlenmeyer, B. Prijs, E. Sorkin, E. Suter, Helv. Chim. Acta, 31, 988 (1948).

[2] R. Hirt, H. Hurni, Helv. Chim. Acta. 32, 378 (1949).

[3] K. Jensen, K. Rosdahl, H. Ingvorsen, Acta Chem. Scand. 2, 220 (1948).

[4] S. Freire, N. Rist, T. Grumback, S. Cals. Comptes. rend. 231, 1004 (1950).

[5] Swiss. 265667, Chem. Abs. 44, 9480 (1950).

[6] See, for example: B. Tozer, S. Smiles, J. Chem. Soc. 1938, 1898.

[7] See, for example: M. P. Gerchuk and S. Z. Taits, J. Gen. Chem. 20, 911 (1950). •

[8] See, for example: M. Viscontini, J. Puldes, Helv. Chim. Acta. 33, 591 (1950).

SYNTHESIS OF HOMOLOGS OF PARAAMINOSALICYLIC ACID

M. N. Shchukina, Yu. V. Markova, and A. M. Pozharskaya

In the comparatively short time since discovery of the antitubercular activity of p-aminosalicylic acid, a large number of studies have been made on synthesis and biological investigation of many of its derivatives and analogs. However, homologs of p-aminosalicylic acid containing an alkyl group on the aromatic nucleus have not been described in the chemical literature until the present time. It seemed of interest to synthesize such compounds in order to investigate the effect of side chains on the anti-tubercular activity of compounds of this type, because the introduction of alkyl groups into the aromatic nucleus of several phenols, for example the derivatives of resorcinol and resorcylic acid, increases their anti-tubercular activity, reaching a maximum with the hexyl-substituted derivative [1].

In the present paper we describe synthesis of the simplest alkyl derivatives of p-aminosalicylic acid — 3-methyl-4-amino-6-hydroxybenzoic acid (I) and 2-hydroxy-4-amino-6-methylbenzoic acid (II):
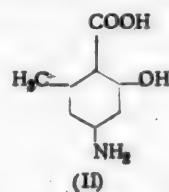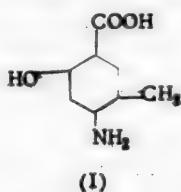
We prepared 3-methyl-4-amino-6-hydroxybenzoic acid (I) starting with p-nitro-o-toluidine, by subjecting its acetyl derivative to catalytic reduction in an ethyl acetate medium in presence of skeletal nickel catalyst. By diazotization accompanied by saponification, 2-acetamido-4-nitrotoluene was converted into 2-amino-4-hydroxytoluene, which was then heated in an autoclave with carbon dioxide and anhydrous potassium carbonate.

The starting material for synthesis of 2-hydroxy-4-amino-6-methylbenzoic acid (II), 3-hydroxy-5-nitrotoluene, was prepared by us from p-acetotoluide via 3,4-dinitro-p-toluidine [2], eliminating the amino group by diazotization [3], reduction to 3-amino-5-nitrotoluene [4], and diazotization [5]. The 3-hydroxy-5-nitrotoluene prepared in this manner was reduced, in the presence of skeletal nickel catalyst in an alcoholic medium, to 3-hydroxy-5-aminotoluene which was then carboxylated under the same conditions as were used for 2-amino-4-hydroxytoluene.

The carboxyl group position in the methyl-p-aminosalicylic acids prepared cannot be given incontravertibly, because theoretical possibilities exist, that carbon dioxide can add in the 3 position to 2-amino-4-hydroxytoluene and in the 4 or 6 positions of 3-hydroxy-5-aminotoluene. However, using results obtained in carboxylation of m-aminophenol, where the carboxyl group predominately adds para to the amino group, we may presume that the carboxyl group is likewise para to the amino group in the acids we prepared, i.e., corresponding to formulas (I) and (II).

EXPERIMENTAL

2-Acetamido-4-aminotoluene. 25 g 2-acetamido-4-nitrotoluene in 100 ml ethyl acetate was hydrogenated in presence of 2.5 g skeletal nickel catalyst in an autoclave at 40° and 60 atm pressure for 1 hour. The reaction product was separated from catalyst, solvent evaporated under vacuum, and the precipitate which separated recrystallized from alcohol. Yield 22.7 g (90.5% of theoretical); m.p. 139-140°.

2-Amino-4-hydroxytoluene. To 10 g 2-acetamido-4-aminotoluene in 10 ml concentrated hydrochloric acid and 75 ml water, we added at 65° a solution of 4.5 g sodium nitrate in 80 ml water during a 30 minute period. The reaction mixture was then heated at 65° for 30 minutes with stirring. The resulting solution was filtered and concentrated under vacuum. 75 ml 25% hydrochloric acid solution was added to the residue and refluxed for 15-20 minutes. The solution was cooled, neutralized with potassium bicarbonate, and extracted

with ether. After drying the ether extract with sodium sulfate, the ether was vaporized, and the residue recrystallized from water. 3.2 g 2-amino-4-hydroxytoluene (about 43% of theoretical) was obtained; m.p. 144-145°.

Carboxylation of 2-amino-4-hydroxytoluene. 2 g 2-amino-4-hydroxytoluene was mixed with 20 g finely divided calcined potassium carbonate; the mixture was heated in an autoclave for 6 hours at oil bath temperature (175-178°) with a 50-60 atm carbon dioxide pressure. After cooling, the reaction product was dissolved in water, treated with sodium hydrosulfite, filtered, and carefully acidified with hydrochloric acid while adequately cooled. The separated acid was filtered by suction, washed with water and purified by solution in sodium bicarbonate with subsequent liberation of the aminoacid by use of acetic acid.

We obtained 2.3 g 2-hydroxy-4-amino-5-methylbenzoic acid (about 85% of theoretical). M.p. 145-146° (with decomposition). Fine needle-like crystals, lightly rose colored. Soluble in bicarbonate, ether, and benzene; poorly soluble in ethyl acetate and cold water.

6.125 mg substance: 0.430 ml N_2 (23°, 743 mm). Found %: N 7.98. $C_8H_9O_3N$. Calculated %: N 8.38.

3-Hydroxy-5-aminotoluene. 10 g 3-hydroxy-5-nitrotoluene (prepared from p-acetotoluide) was dissolved in 60 ml ethyl alcohol and hydrogenated in presence of 6 g skeletal nickel catalyst at normal pressure and room temperature. After removal of catalyst and vaporization of alcohol under vacuum, the residue was treated with 10% hydrochloric acid. The free base was separated from the resulting solution of 3-hydroxy-5-aminotoluene hydrochloride by addition of dry sodium bicarbonate. After washing with water and drying in a vacuum dessicator, we obtained 5.1 g 3-hydroxy-5-aminotoluene. M.p. 137-138°. Needles, very rapidly turning dark violet. The material was readily soluble in hot water, alcohol and acetone; poorly soluble in ether; and insoluble in benzene.

6.270 mg substance: 0.628 ml N_2 (28°, 725 mm). Found %: N 10.84. C_7H_9ON. Calculated %: N 11.38.

The substance was not purified further in view of its ease of oxidation.

Carboxylation of 3-hydroxy-5-aminotoluene. A mixture of 2 g 3-hydroxy-5-aminotoluene and 20 g calcined potassium carbonate was heated for 7-8 hours in an autoclave at 170-180° with a 50-60 atm carbon dioxide pressure. After cooling, the contents of the tube were dissolved in water and carefully acidified with hydrochloric acid. The separated acid was filtered by suction, washed with water, and purified by conversion into the sodium salt by action of an aqueous solution of sodium bicarbonate followed by subsequent separation of the free acid by treating the sodium salt with hydrochloric acid. We obtained 1.85 g 2-hydroxy-4-amino-6-methylbenzoic acid. M.p. 127.5-128°. The material decarboxylated at its melting point.

It was soluble in bicarbonate, chloroform, petroleum ether, and benzene; poorly soluble in ether, ethyl acetate, and cold water.

7.010 mg substance: 0.539 ml N_2 (27°, 725.5 mm). Found %: N 8.54. $C_8H_9O_3N$. Calculated %: N 8.38.

SUMMARY

2-Hydroxy-4-amino-5-methylbenzoic acid was synthesized via a series of intermediate materials starting from 2-amino-4-nitrotoluene. 2-Hydroxy-4-amino-6-methylbenzoic acid was prepared starting with 3-hydroxy-5-nitrotoluene.

LITERATURE CITED

[1] H. D. Vorgelsang, Th. Wagner-Yauregg, Ann. 568, 116 (1950); E. Klarmann, J. Am. Chem. Soc., 55, 2576 (1933).

[2] R. A. Morton, A. McGookin, J. Chem. Soc. 1934, 910.

[3] J. B. Cohen, D. McCandlisch, J. Chem. Soc. 87, 1271 (1905).

[4] W. Staedel, Ann. 217, 199 (1883).

[5] R. D. Haworth, A. Lapworth, J. Chem. Soc. 1923, 2990.

AMIDINES OF AMINO ACIDS

1. SYNTHESIS OF IMINO-ETHERS OF AMINO ACIDS

A. N. Baksheev* and N. I. Gavrilov

Representatives of many types of imino-ethers are known: aromatic, aliphatic, and heterocyclic, with various functional and hydrocarbon substituents on the radical R. The classical method for synthesis of these compounds, which enabled preparation of the overwhelming majority of imino-esters referred to, involves treatment of an equimolar mixture of the proper nitrile and absolute alcohol with dry hydrogen chloride [1]:

$$RCN + R'OH + HCl \longrightarrow R-C\begin{array}{c} NH \cdot HCl \\ OR'. \end{array}$$
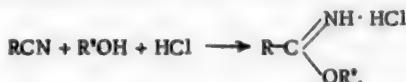
As a rule, the imino-ether salts produced as a result of the reaction are colorless crystalline compounds which readily react with various substances (water, alcohol, amines, etc.). Because of their high reactivity, excess alcohol must be avoided in preparation of imino-ether salts, very carefully dried reagents must be used, and the reaction must be performed at sufficiently low temperatures.

However, despite wide applicability of this method for synthesis of many imino-ethers, it is not generally possible to prepare imino-ethers of amino acids from the corresponding amino-nitriles in this manner. This is explained, in most cases, by the slight solubility of amino-nitrile salts in alcohol (in treating a mixture of equimolar quantities of amino-nitrile and alcohol with hydrogen chloride, as is required by this method, an amino-nitrile salt forms at first which precipitates from solution and very incomplete conversion to imino-ether occurs [2]). The situation is not improved by use of other non-hydroxy-containing solvents (benzene, chloroform, ether), because amino-nitrile salts are likewise poorly soluble in them usually; (in fact, use of similar solvents proved successful in synthesis of N-acyl derivatives of amino acid imino-ethers [3,5]). In this connection one should mention the work of Curcius [4]. The latter, treating aminoacetonitrile with a large excess of absolute ethyl alcohol saturated with hydrogen chloride, was able to show that the precipitate which spontaneously separated from the reaction mixture was aminoacetiminoethyl ether dihydrochloride:
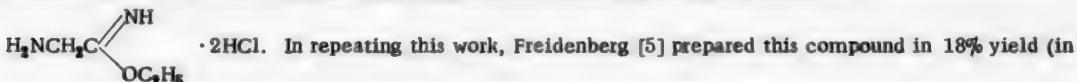
$H_2NCH_2C\begin{array}{c} NH \\ OC_2H_5 \end{array}$ · 2HCl. In repeating this work, Freidenberg [5] prepared this compound in 18% yield (in

contrast to the 40% yield reported by Curtius). The low yield was due to the relatively poor solubility of aminoacetonitrile hydrochloride in an alcoholic solution of hydrogen chloride, because of which some of the starting material was recoverable unchanged.

We found that aminoacetiminoethyl ether could be easily prepared with a significantly good yield (80%) by using excess of methyl alcohol saturated with hydrogen chloride to ensure complete solubility of the initial aminoacetonitrile hydrochloride. However, a similar procedure for homologs of aminoacetonitrile did not as a rule lead to spontaneous precipitation of the imino-ether salt, as was observed in the above instance; consequently, we decided to use a small excess of ethyl ether to precipitate the reaction product, based on the almost complete insolubility of imino-ether salts in this solvent.

In using this method, questions inevitably arose on whether the length of reaction time (prior to precipitation by ether) was suitable and whether, in principle, it was possible to obtain sufficiently pure material by this method (purification of imino-ether salts, because they are so labile, is a difficult operation associated with large losses). It was necessary to consider whether salts of the initial amino-nitrile (if reaction were incomplete), or decomposition products of the imino-ether, would be separated together with the imino-ether salt on addition of ether to the reaction mixture.

---

* Deceased.

Tests were performed [using the dihydrochloride of dimethylaminoacetonitrile, $(CH_3)_2NCH_2CN$, as a starting material for a series of experiments] which showed that almost complete conversion of the initial nitrile into an imino-ether occurred in a 10 minute reaction time. Product purity was not decreased with a one hour reaction time, but increasing the time to 3 hours significantly reduced imino-ether purity. Further extension of the reaction period resulted in complete decomposition of the imino-ether salt (Table 2). Using this improved method, we were able to prepare, as dihydrochlorides, the following a-amino acid imino-ethers: aminoacetiminomethyl ether $H_2NCH_2C\overset{NH}{\underset{OCH_3}{<}}$, dimethylaminoacetiminomethyl ether

$(CH_3)_2NCH_2C\overset{NH}{\underset{OCH_3}{<}}$, dimethylaminoacetiminoethyl ether $(CH_3)_2NCH_2C\overset{NH}{\underset{OC_2H_5}{<}}$, alanineiminomethyl ether

$H_2NCH(CH_3)C\overset{NH}{\underset{OCH_3}{<}}$, N-phenylglycineiminomethyl ether $C_6H_5HNCH_2C\overset{NH}{\underset{OCH_3}{<}}$, and aminoisobutyriminomethyl

ether $H_2NC(CH_3)_2C\overset{NH}{\underset{OCH_3}{<}}$.
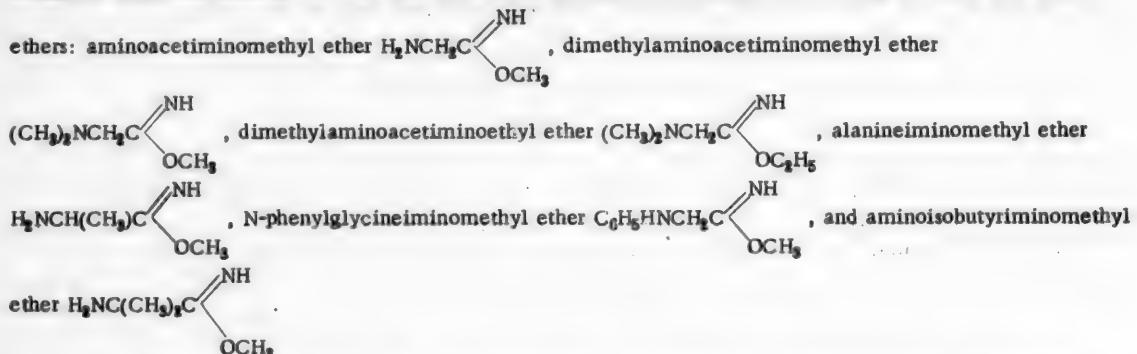
The compounds we prepared were colorless crystalline materials, which decomposed rather readily to the corresponding amides on storage. This was particularly rapid for dimethylaminoacetiminoethyl ether hydrochloride. To follow imino-ether decomposition qualitatively as it occurred, we used this test: addition of a copper salt solution together with a small quantity of alkali to freshly prepared imino-ether gave a blue solution; the more the imino-ether decomposed into the corresponding amide, the more and more violet was the solution color on addition of these reagents, reaching a lilac-violet with amides.

Because of the reactivity and instability of these compounds a number of precautions were necessary for their synthesis, namely: isolation from atmospheric moisture and absolute dryness of the reagents (alcohol, ether). Instability of these compounds with time forced us to conduct their analysis, and to perform further studies, immediately on preparation, after drying in a vacuum dessicator over sulfuric acid or solid sodium hydroxide.

In preparing imino-ether salts from β-dimethylaminopropionitrile under the same conditions as were used for an a-aminonitrile, we noted that the former reacted noticeably more slowly: using a 10 minute reaction time, material separated after addition of ether contained a considerable portion of unchanged nitrile salt; only by increasing the reaction time to one half hour were we able to obtain the desired imino-ether in sufficiently high yield.

The difference in the rate of formation of imino-ethers of a- and β-aminonitriles undoubtedly is caused by activation of the nitrile group of the former by the adjacent a-amino group. The effect of the latter in β-dimethylaminopropionitrile, in consequence of the greater separation, must be regarded as being at a comparatively lower level. An instance of similar activation, but to higher levels, was shown by the compound trichloracetonitrile, which gave the corresponding imino-ether on treatment with alcohol (without use of hydrogen chloride) [6], — this reaction is not known for ordinary nitriles.

By applying our improved method to an aromatic aminonitrile —m-aminobenzonitrile —we were able to prepare m-aminobenziminomethyl ether dihydrochloride: $H_2NC_6H_4C\overset{NH}{\underset{OCH_3}{<}}$ · 2HCl.
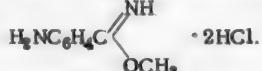
Thus, the above method of synthesis may be regarded as sufficiently general for preparation of imino-ethers of amino acids; in actual fact, like the classical method, it has several limitations. For example, in attempts to convert a-phenylglycinenitrile into the corresponding imino-ether, instead of the latter, the hydrochloride of a-phenylglycineamide $H_2NCH(C_6H_5)C\overset{O}{\underset{NH_2}{<}}$ was separated quantitatively. This

phenomenon was also observed in tests to prepare imino-ethers of certain a-substituted nitriles by the classical method. Steinkopf [7], who also investigated a series of substituted acetonitriles from this same point of view, obtained, by carrying out the reaction, the results given in Table 1.

TABLE 1

Compound	Result of reaction
ClCH$_2$CN	
BrCH$_2$CN	Imino-ether salt
ICH$_2$CN	
O$_2$NCH$_2$CN	
Cl$_3$CCN	
Br$_3$CCN	Amide
Cl$_2$CHCN	
O$_2$NCCl$_2$CN	
Br$_2$CHCN	Mixture of Amide and imino-ether salt
O$_2$NC(CH$_3$)$_2$CN	Imino-ether salt

The data definitely show that the reaction products are determined both qualitatively and quantitatively by the negative substituents; this was also noted by Steinkopf.

The anomalous result obtained by us in attempting to prepare an imino-ether salt from phenylglycinenitrile is in accordance with this data: introduction of a phenyl group into nitrile molecule which already has an electronegative substituent in the α-position — the amino group — increases the effect of the latter sufficiently strongly so that the reaction leads to formation of amides instead of imino-ether salts.

Replacement of the phenyl group by a methyl group, which has an electropositive character, results, as might have been expected, in formation of normal reaction products — imino-ether salts (alanine-iminomethyl ether).

Undoubtedly, the difference in reaction course between nitro-acetonitrile and nitroisobutyronitrile may be explained in a similar manner (Steinkopf was inclined to regard the possible existence of the nitro group of the former in an aci-form as the reason for the difference), namely, the presence of two methyl groups in the nitroisobutyronitrile molecule compensates for the electronegative effect of the nitro group to such an extent that imino-ethers are formed during the reaction.

EXPERIMENTAL

I. Aminoacetiminomethyl (glycineiminomethyl)-ether

Methyleneaminoacetonitrile [8]. This was prepared from 270 g ammonium chloride, 750 g formalin (specific gravity 1.078), and 245 g sodium cyanide. Yield 225 g. After recrystallization from water it melted at 128.5-129°.

Aminoacetonitrile hydrochloride [4]. This was made by treating 10 g methyleneaminoacetonitrile with 150 ml of a 1 N solution of hydrogen chloride in ethyl alcohol. 8.5 g of the nitrile salt were separated. Another 4 g of the substance were separated from the mother liquor using ether. Methyl alcohol may be used in preparation of the substance instead of ethyl alcohol: 22 g methyleneaminoacetonitrile was wetted with a small quantity of methyl alcohol and 170 ml of a 2 N solution of hydrogen chloride in methyl alcohol gradually added with stirring. The material rapidly went into solution, and the mixture was permitted to stand for a day. The crystals which had separated in that time were removed by suction filtration, washed with ether, and dried in a vacuum dessicator. Yield 19.5 g (63.5% of theoretical). An additional 7-8 g of material could be recovered by concentration of the mother liquor or by addition of ether. Recrystallization from five times its volume of methyl alcohol gave a pure product, m.p. 173-175° (with decomposition).

Exclusion of atmospheric moisture was essential in working with aminoacetonitrile hydrochloride because the substance was highly hygroscopic.

Aminoacetiminomethyl ether dihydrochloride. 2 g aminoacetonitrile hydrochloride was triturated with a small amount of absolute methyl alcohol (protected from atmospheric moisture); to this was added, with simultaneous cooling, 50 g absolute methyl alcohol which had been saturated with dry hydrogen chloride at 10°. Rapid solution occurred on vigorous agitation, and in 2-3 minutes a voluminous precipitate began to form. When precipitation begins the nitrile salt should be almost completely dissolved; this is normally the case if trituration is thorough; otherwise the solution should be quickly filtered under reduced pressure with atmospheric moisture excluded. It was most convenient to perform the reaction in a N. I. Gavrilov apparatus (see sketch); this apparatus is fitted with a calcium chloride tube and has an integral filter which may be connected to a vacuum receiver. The filter plate had to be rather porous (no.1-2). The precipitate which formed in an hour was filtered, washed with absolute ether, and dried in a vacuum dessicator. Yield 2.6 g (80% of theoretical). M.p. 198-199° (with decomposition).

0.1828 g, 0.2114 g substance: 22.85 ml, 26.40 ml 0.1 N H$_2$SO$_4$ (Kjeldahl). 0.1972 g, 0.2008 g substance: 24.0 ml, 25.00 ml 0.1 N AgNO$_3$ (Volhard). Found %: N 17.49, 17.48; Cl 44.28, 44.19. C$_3$H$_{10}$ON$_2$Cl$_2$. Calculated %: N 17.39; Cl 44.10

Colorless flakes, readily soluble in water with evolution of heat. It was difficultly soluble in alcohol and insoluble in ether.

After three weeks storage, recrystallization of the imino-ether salt from methyl alcohol gave colorless crystals with m.p. 207-208°. Both before and after recrystallization this substance gave an intense violet color when treated with copper salts in alkaline solution. This material was soluble in water without evolution of heat, poorly soluble in alcohol, and insoluble in ether.

0.1460 g, 0.1749 g substance: 26.3 ml, 31.4 ml 0.1 N H_2SO_4. (Kjeldahl). 0.1832 g substance: 16.55 ml 0.1 N $AgNO_3$ (Volhard). Found %: N 25.22, 25.13; Cl 32.07. $C_2H_7ON_2Cl$. Calculated %: N 25.22, 25.13; Cl 32.12.

The material thus was aminoacetamide hydrochloride as shown by its properties and the analytical data (m.p. 186-189° [9]).

II. Dimethylaminoacetiminomethyl ether

Dimethylaminoacetonitrile. This was prepared from 110 ml 22.8% aqueous dimethylamine solution, 50 ml formalin, and 30 g potassium cyanide. The yield of the nitrile was 26 g, m.p. 135-138°. By treatment of dimethylaminoacetonitrile in ether solution with hydrogen chloride, we prepared the nitrile salt, which after recrystallization from methyl alcohol had a m.p. of 150-151.5°.

Ground hollow

Fritted glass plate

Gavrilov Apparatus

Dimethylaminoacetiminomethyl ether dihydrochloride. To 3 g dimethylaminoacetonitrile hydrochloride was added 50 ml absolute methyl alcohol which had been saturated cold (cooled with ice water) with dry hydrogen chloride. The reaction mixture was shaken, and after complete solution of the nitrile salt occurred (which generally took 2-3 minutes), was permitted to stand for 20 minutes. At the end of this time, twice the volume of absolute ether was added; this produced a voluminous precipitate. The latter was allowed to stand for a half-hour and filtered by suction, washed with absolute ether, and dried in a vacuum dessicator. Yield 3.7 g (79% of theoretical), colorless solid with a mother-of-pearl luster. M.p. 195-197°.

0.2112 g substance: 22.50 ml 0.1 N H_2SO_4 (Kjeldahl) 0.2188 g, 0.2010 g substance: 23.25 ml, 21.35 ml 0.1 N $AgNO_3$ (Volhard). Found %: N 14.91; Cl 37.72, 37.7. $C_5H_{14}ON_2Cl_2$. Calculated %: N 14.81; Cl 37.62.

The substance was readily soluble in water (with decomposition) and less soluble in methyl alcohol.

After lengthy storage, the substance when recrystallized from methyl alcohol yielded colorless crystals with m.p. 206-207°, which were readily soluble in water and methyl alcohol and insoluble in ether. A violet color was obtained by treatment of this material with an aqueous solution of divalent copper in the presence of alkali.

6.035 mg, 4.825 mg substance: 7.605 mg, 6.100 mg CO_2; 4.335 mg, 3.390 mg H_2O. Found %: C 34.37, 34.48; H 8.03, 7.88. $C_4H_{11}ON_2Cl$. Calculated %: C 34.65; H 7.97.

It therefore appeared that this material was dimethylaminoacetamide hydrochloride.

Effect of increase in time for reaction of methyl alcohol (saturated with hydrogen chloride) and dimethyl-aminoacetonitrile hydrochloride on dimethylaminoacetiminomethyl ether dihydrochloride formation. In order to study the velocity of imino-ether formation as well as their stability in the reaction mixture with time, we performed a series of tests in which we varied reaction time holding all other conditions constant. In these tests, we treated 2 g dimethylaminoacetonitrile hydrochloride with 35 ml absolute methyl alcohol which had been saturated cold (cooled with ice water) with hydrogen chloride. The reaction mix was agitated, with cooling, until the starting nitrile salt was dissolved and was let stand in ice water for a predetermined time, at the end of which we added double the volume of absolute ether to precipitate the reaction product. The reaction mixture was maintained cold

TABLE 2

Reaction Time	Yield of imino-ether salt (in grams)	Analysis of reaction product (in %)		Notes
		Nitrogen (Kjeldahl)	Chlorine (Volhard)	
10 minutes	2.5	14.61	37.72	
1 hour	2.6	14.78	37.58	Theoretical
3 hours	2.5	15.15	37.6	composition:
7 hours	1.9	18.82	31.86	Cl 37.6%
				N 14.81%
20 hours	On addition of ether, ammonium chloride was quantitatively separated			

in ice water for 0.5-1 hour, depending on the ease of separation of the precipitate; the latter was then filtered by suction, washed several times with absolute ether and dried in a vacuum dessicator for 3 hours. All of these operations were performed with atmospheric moisture excluded. Samples for analysis were taken immediately after drying.

Reaction times (after solution of the nitrile salt) were: 10 minutes, 1,3,7, and 20 hours. Test data are given in Table 2.

III. Dimethylaminoacetiminoethyl ether dihydrochloride.

20 ml absolute ethyl alcohol which had been saturated cold with dry hydrogen chloride was added to 1 g dimethylaminoacetonitrile hydrochloride. On continued stirring with cooling, the nitrile salt gradually went into solution. Solution took place considerably more slowly than in preparation of the methyl homolog, and was complete in about a half-hour. After the solution had stood for an hour (cooled in ice water), we added twice its volume of absolute ether; a colorless oil, which gradually became completely crystalline, soon began to separate on the bottom of the reaction vessel. After suction filtration and washing with absolute ether, we obtained 1.35 g (81% of theoretical) of colorless hygroscopic crystals.

The material reacted with water with liberation of heat, and rapidly decomposed on storage in a vacuum dessicator; the freshly prepared substance did not form a violet copper complex, but after 1-2 hours of storage the violet color of the complex was clearly evident (transformation into dimethylaminoacetamide). Because it was not possible to analyze this substance for the above reason, we demonstrated that it was really dimethylamino-acetaminoethyl ether dihydrochloride by treating 1 g of freshly prepared substance with a solution of 1 ml dry aniline in 10 ml ether. The precipitate quickly re-formed, turned to a viscous liquid and then solidified again; the reaction mix was allowed to stand for 2 days after which the precipitate was filtered by suction and washed with ether. Yield 1.25 g. This material was dissolved in methyl alcohol and subsequently precipitated with ether to yield a substance which gave, with an alcoholic solution of picric acid, yellow crystals, having m.p. 217-218°, which did not depress the melting point of N-phenyldimethylaminoacetamidine dipicrate.

IV. Aminoisobutyriminomethyl ether.

Aminoisobutyronitrile hydrochloride [11]. Aminoisobutyronitrile was prepared from 55 g ammonium chloride, 74 ml acetone, and 70 g potassium cyanide. Yield 43 g; m.p. 70-71°.

Aminoisobutyronitrile hydrochloride was prepared by passing hydrogen chloride into an ether solution of the nitrile until it reacted acid to Congo red. M.p. 147-149°. If necessary, the substance was recrystallized. For this we dissolved it in a small quantity of methyl alcohol and then added 4 times its volume of acetone; very well-formed crystals of aminoisobutyronitrile hydrochloride gradually began to separate.

Aminoisobutyroiminomethyl ether dihydrochloride. We added 35 ml absolute methyl alcohol which had been saturated when cold with hydrogen chloride to 2 g aminoisobutyronitrile hydrochloride. On continued cooling in ice water, with stirring, the nitrile salt quickly went into solution (2-3 minutes), and the reaction mixture was allowed to stand for 15 minutes. Three times its volume of absolute ether was added, and a colorless oily liquid, which became completely crystalline in several minutes, rapidly separated. After a half-hour the residue was filtered by suction, washed three times with absolute ether, and dried in a vacuum dessicator. Yield 2.6 g (82.5% of theoretical). M.p. 244-247° (with decomposition). It was soluble in water with the evolution of heat.

0.2031 g, 0.2120 g substance: 20.95 ml, 22.00 ml 0.1 N H_2SO_4 (Kjeldahl). 0.2250 g, 0.2350 g substance: 23.47 ml, 24.60 ml 0.1 N $AgNO_3$ (Volhard). Found %: N 14.44, 14.52; Cl 37.03, 37.16. $C_6H_{14}ON_2Cl_2$. Calculated %: N 14.81; Cl 37.62.

V. N-Phenylglycineiminomethyl ether

N-Phenylglycinenitrile hydrochloride [12]. We prepared N-phenylglycinenitrile from 32 ml formalin (specific gravity 1.078), 37 ml aniline, and 40 g potassium cyanide. Yield 41 g, light yellow crystals with m.p. 44-45°. After recrystallization from ether we obtained almost colorless crystals, m.p. 47-48°.

The nitrile hydrochloride was prepared by dissolving the nitrile in ether and adding a saturated solution of hydrogen chloride in alcohol until reaction was acid to Congo red. The precipitate which separated was filtered by suction, washed with ether, and recrystallized from ethyl alcohol. Colorless crystals which decomposed without melting when heated to 200°.

N-Phenylglycineiminomethyl ether dihydrochloride. 50 ml absolute methyl alcohol which had been saturated cold with hydrogen chloride was added to 3 g finely crushed N-phenylglycinenitrile hydrochloride. The nitrile salt went into solution after about 3-5 minutes of agitation with cooling, and soon thereafter the imino-ether salt began to separate. The residue was filtered by suction after 1.5 hours, washed several times with absolute ether, and dried in a vacuum dessicator. Colorless crystals; m.p. 185-186°. Yield 3.0 g (71.5% of theoretical). The material was soluble in water, and poorly soluble in ethyl alcohol.

0.1952 g, 0.2004 g substance: 16.0 ml, 16.85 ml, 0.1 N. H_2SO_4 (Kjeldahl). 0.2002 g, 0.2246 g substance: 16.85 ml, 18.70 ml 0.1 N. $AgNO_3$ (Volhard). Found %: N 11.91, 11.77; Cl 29.88, 29.56. $C_9H_{14}ON_2Cl_2$. Calculated %: N 11.82; Cl 29.95.

VI. Attempted preparation of α-phenylglycineiminomethyl ether.

α-Phenylglycinenitrile hydrochloride. We prepared this from 10 g benzaldehyde, 10 g potassium cyanide, and 5 g ammonium chloride, following N.D. Zelinsky and G. L. Stadnikov [13]. Yield 9.8 g, slightly yellowish crystals. The dried and crushed substance was treated several times with chloroform and then washed several times with ether; this gave a product which was free of color. M.p. 175-176°.

Attempted preparation of α-phenylglycineiminomethyl ether dihydrochloride. 60 ml absolute methyl alcohol which had been saturated cold with hydrogen chloride was added to 3 g α-phenylglycinenitrile hydrochloride. On continued agitation with cooling, the nitrile salt finished going into solution in 6-8 minutes. After cooling for 10 minutes in ice water, we added 3-4 times its volume of absolute ether; if the temperature of the reaction mixture was sufficiently low, precipitation did not noticeably begin at this time, and the mixture was let stand overnight. The finely crystalline precipitate which separated during this time was filtered by suction, washed with ether, and dried in a vacuum dessicator. Yield 3.2 g. M.p. 272-273°. Poorly soluble in alcohol; insoluble in ether and chloroform. An aqueous solution of the substance developed a violet color with copper salts and alkali.

Recrystallization from water gave colorless crystals, with m.p. 280-281° (with decomposition), which retained the property of the un-recrystallized material to give a violet-colored copper complex.

3.295 mg, 3.108 mg substance: 6.267 mg, 5.898 mg CO_2; 1.645 mg H_2O. 4.195 mg, 2.867 mg substance: 0.549 ml, 0.375 ml N_2 (22.50°, 745 mm). Found %: C 51.90, 51.79; H 6.06, 5.92; N 14.85, 14.81. $C_8H_{11}ON_2Cl$. Calculated %: C 51.47; H 5.89; N 15.01.

From this it appears that the reaction product was not α-phenylglycineiminomethyl ether, dihydrochloride but rather α-phenylglycineamide hydrochloride.

VII. Alanineiminomethyl ether.

Alaninenitrile hydrochloride [14]. We prepared alaninenitrile from 26.6 g ammonium chloride, 10 g acetaldehyde, and 29.5 g potassium cyanide. Hydrogen chloride was passed through an ether solution of the nitrile until the solution was acid to Congo red. The yellowish-white precipitate which separated was filtered by suction, washed with ether, and dried in a vacuum dessicator. Yield 23 g. M.p. 126-128°. (According to the literature the m.p. is 115-117° [15] and 132-133° [16]).

As a consequence of the difficulty of purifying the substance, it was used in the next stage without further treatment.

Alanineiminomethyl ether dihydrochloride. 35 ml absolute methyl alcohol which had been saturated cold with hydrogen chloride was added to 2 g alaninenitrile hydrochloride. The nitrile salt dissolved in intermittent agitation while cooling in ice-water, and after a half-hour absolute ether was added to the solution until turbidity was not

cleared up by shaking; the mixture was then let stand for one and one-half hours while cooling in ice water. The precipitate which separated was filtered by suction, washed with ether, and dried in a vacuum dessicator. Yield 2 g (60.5% of theoretical), slightly yellowish hygroscopic material, liberates heat when dissolved in water. The material was poorly soluble in ethyl alcohol, somewhat more soluble in methyl alcohol, and insoluble in ether and chloroform.

> 0.2132 g, 0.1976 g substance: 23.6 ml, 22.4 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1938 g, 0.1640 g substance: 21.40 ml, 18.00 ml 0.1 N $AgNO_3$ (Volhard). Found %: N 15.50, 15.87; Cl 39.20, 38.96. $C_4H_{12}ON_2Cl_2$. Calculated %: N 16.00; Cl 40.6.

The analytical results were somewhat low and the material was somewhat colored, no doubt because of incompletely pure initial nitrile; however, there is no doubt that the material was the desired imino-ether.

VIII. β-Dimethylaminopropioniminomethyl ether.

35 ml absolute methyl alcohol which had been saturated when cold with dry hydrogen chloride was added to 2 g β-dimethylaminopropionitrile hydrochloride (m.p. 203-204°). The starting nitrile salt dissolved in 2-3 minutes of shaking, while cooled in ice-water. After 10 minutes the reaction mix was diluted with one and one-half times its volume of absolute ether. The finely crystalline white precipitate (1.5 g) which separated at once appeared to be unchanged aminonitrile salt. On extension of the reaction time to one-half hour, addition of one and one-half volumes of absolute ether gave a transparent solution on shaking from which colorless fine prisms separated gradually on standing when cold. After 2 hours the residue was filtered by suction, washed with ether, and dried in a vacuum dessicator. Yield 2.3 g (76% of theoretical). On heating the material effervesced and decomposed at about 100°. Readily soluble in water, less soluble in methyl alcohol.

> 0.2012 g, 0.2238 g substance: 20.1 ml, 22.15 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1904 g, 0.2319 g substance: 18.75 ml, 23.0 ml 0.1 N $AgNO_3$ (Volhard). Found %: N 13.96, 13.86; Cl 34.95, 35.20. $C_6H_{14}ON_2Cl_2$. Calculated %: N 13.80; Cl 34.97.

IX. m-Aminobenziminomethyl ether.

m-Nitrobenzonitrile [17]. This was prepared from 25 g m-nitroaniline, 12.5 g sodium nitrite, 45 g copper sulfate, and 51 g potassium cyanide. Light yellow crystals with m.p. 113-114° (m.p. 117° [17]). Yield 8 g. Because of large losses in purification, the prepared substance was used in the next stage without further treatment.

m-Aminobenzonitrile [17]. We prepared this from 8 g m-nitrobenzonitrile by reduction with 48 g stannous chloride. Yield 45 g; slightly yellowish crystals with m.p. 49° (m.p. 53-53.5° [17].

The nitrile was purified via its hydrochloride. For this, we gradually added, with cooling, ether, which had been saturated with hydrogen chloride, to an ether-alcohol solution of the substance. The white precipitate of m-aminobenzonitrile hydrochloride was filtered by suction, washed with ether, and then twice recrystallized from methyl alcohol. Colorless crystals, m.p. 209-210°.

m-Aminobenziminomethyl ether dihydrochloride. 15 ml absolute methyl alcohol, saturated when cold with hydrogen chloride, was added to 0.5 g m-aminobenzonitrile hydrochloride. The reaction mixture was allowed to stand at room temperature with periodic shaking. Solution of the nitrile salt was complete in about a half-hour, and in a short while the solution then began to deposit a fibrous, cotton-like, colorless precipitate. The mixture was cooled in ice for 1.5 hours, the residue was then filtered by suction, washed several times with ether, and dried in a vacuum dessicator. Yield 0.45 g (62% of theoretical). M.p. 238-240° (with decomposition). Using ether, we were able to separate an additional quantity of material from the same mother liquor.

Light colorless thread-like crystals which were difficultly soluble in methyl alcohol and readily soluble in water without displaying significant thermal effect.

> 0.1486 g substance: 13.1 ml 0.1 N H_2SO_4 (Kheldahl). 0.1534 g substance: 13.8 ml 0.1 N $AgNO_3$. (Volhard). Found %: N 12.35; Cl 31.93. $C_8H_{12}ON_2Cl_2$. Calculated %: N 12.55; Cl 31.83.

SUMMARY

1. A method was developed for synthesis of imino-ethers of α-amino acids and its applicability for synthesis of aromatic and β-series imino-ethers demonstrated.

2. It was shown that formation of these compounds takes place quickly and completely, and that the imino-ether formed is relatively stable, in presence of alcohol saturated with hydrogen chloride. This enabled separation of

reaction products in a sufficiently pure form without resorting to additional purification. The effect of the amino group location on the velocity of formation of imino-ethers was noted for α- and β-amino acids.

3. The following group of new imino-ethers of α-amino acids was prepared: aminoacetiminomethyl ether, dimethylaminoacetiminomethyl ether, dimethylaminoacetiminoethyl ether, aminoisobutyroiminomethyl ether, alanineiminomethyl ether, and α-phenylglycineiminomethyl ether.

A representative aromatic ether (m-aminobenziminomethyl ether) and a β-type ether (dimethylaminopropiominomethyl ether) were analogously prepared.

Consequently, the proposed method may be regarded as a sufficiently general method for synthesis of amino acid imino-ethers.

LITERATURE CITED

[1] A. Pinner, Ber., 10, 1889 (1871).

[2] A. Pinner, Imidoäther und ihre Derivate, Berlin chpt. 5 (1892).

[3] W. Bachmann, M. Cronyn, The Chemistry of Penicillin, page 879 (1949).

[4] T. Curcius, Ber., 31, 2489 (1898).

[5] K. Freudenberg, H. Eichel, F. Leitet, Ber., 65B, 1183 (1932).

[6] W. Steinkopf, Ber., 40, 1643 (1907).

[7] W. Steinkopf, W. Malinowski, Ber., 44, 2898 (1911).

[8] Organic Synthesis, volume I, page 126.

[9] Bergell, Wulfing, Z. Phys. Chem., 64, 353; Beilstein, IV.

[10] R. Turner, J. Am. Chem. Soc., 68, 1607 (1946).

[11] L Dubsky, Wensink, Ber., 49, 1136 (1916).

[12] Knovenagel, Merklin, Ber., 37, 4081 (1904).

[13] N. D. Zelinsky and G. L. Stadnikov, J. Russ. Chem. Soc., 38, 725 (1906).

[14] L Dubsky, Ber., 49, 1048 (1916).

[15] N. D. Zelinsky and G. L. Stadnikov, J. Russ. Chem. Soc. 40, 792 (1908).

[16] Delepine, Bl. Soc. chim, (3), 29, 1183; Beilstein, IV.

[17] M. Bogert, H. Beems, J. Am. Chem. Soc., 26, 468 (1904).

AMIDINES OF AMINO ACIDS. II

A. N. Baksheev* and N. I. Gavrilov

The wide variety of applications and valuable properties of amidines — compounds having the general formula $R-C\!\!\begin{array}{c}NR_I\\\\NR_{II}R_{III}\end{array}$ (R, R_I, R_{II}, R_{III} = H or organic radicals) — fully justifies the considerable interest chemists have shown in them, which has been reflected by the extensive literature, chiefly in patents, associated with these compounds. Among the many different compounds of this class, amidines of amino acids (where R is an aminoalkyl group) have been described very slightly. But precisely these compounds (mainly amidines of α-amino acids), apart from their possible practical utilization, are of fundamental interest from the point of view of the structure of albumin, as introduced by N.D. Zelinsky and N.I. Gavrilov [1]; consequently, successful synthesis of these compounds is of unconditional interest. For preparation of these compounds we selected a method based on reacting imino-ether salts with amines, which would lead, as a rule, to di-substituted compounds.

$$R-C\!\!\begin{array}{c}NH\\\\OR_I\end{array}\cdot HCl + 2NH_2R_{II} \rightarrow R-C\!\!\begin{array}{c}NR_{II}\\\\NHR_{II}\end{array}\cdot HCl + R_IOH + NH_3.$$
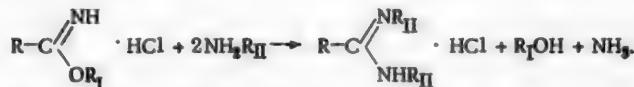
The hydrochlorides of the amino acid imino-ethers necessary were prepared by a previously described method [2]. We used the ordinary procedure, described in the literature, for preparation of the amidines; a mixture of imino-ether salt and amine in solvent (we used absolute ether) was allowed to stand at room temperature for 1-3 days, and the amidine hydrochloride which formed was then separated by a suitable procedure. Since it might be expected that imino-ethers of amino acids with a primary amino group would react in a complex way with aliphatic amines, caused by participation of the amino group of the aminoimino-ether, and because of the unavoidable interchange of hydrogen chloride between the amino groups of the imino-ether and the reacting amine, we used an amine with reduced basicity-aniline. In this way we prepared, from the corresponding imino-ether salts, the following amidines as dihydrochlorides:

N-phenyl-dimethylaminoacetamidine: $(CH_3)_2NCH_2C\!\!\begin{array}{c}NH\\\\NHC_6H_5\end{array}$;

N-phenyl-aminosiobutyramidine: $H_2NC(CH_3)_2C\!\!\begin{array}{c}NH\\\\NHC_6H_5\end{array}$;

N-phenyl-aminoacetamidine: $H_2NCH_2C\!\!\begin{array}{c}NH\\\\NHC_6H_5\end{array}$.
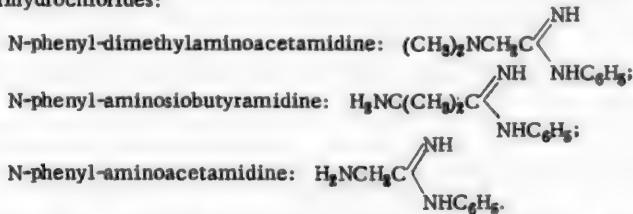
Using the property of dimethylaminoacetamidines to form dipricrates which crystallize well and are difficultly soluble in alcohol (this was used for separation of N-benzyl-dimethylaminoacetamidine in the pure form) we were able to simplify somewhat the method of preparation in some cases: a solution of amine picrate in methyl alcohol was added to the hydrochloride of the imino-ether mentioned; the solution quickly became homogeneous and then, after several minutes, the amidine salt began to separate. In this way we were able to prepare the dipicrates of the following compounds in addition to that of the above mentioned N-phenyl-dimethylaminoacetamidine:

N-glycyl-dimethylaminoacetamidine: $(CH_3)_2NCH_2C\!\!\begin{array}{c}NH\\\\NHCH_2COOH\end{array}$;

N-glycylglycyl-dimethylaminoacetamidine: $(CH_3)_2NCH_2C\!\!\begin{array}{c}NH\\\\NHCH_2CONHCH_2COOH\end{array}$;

---

* Deceased

N-dl-alanylglycylglycyl-dimethylaminoacetamidine:$(CH_3)_2NCH_2C\!\!\begin{array}{l}\diagup NH\\\diagdown NHCH(CH_3)CONHCH_2CONHCH_2COOH.\end{array}$
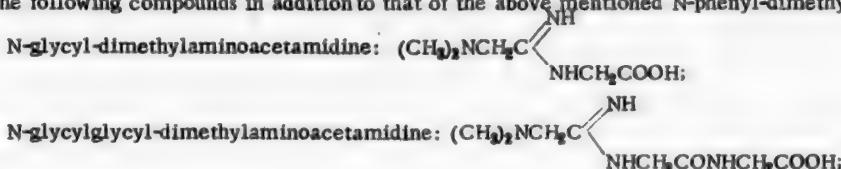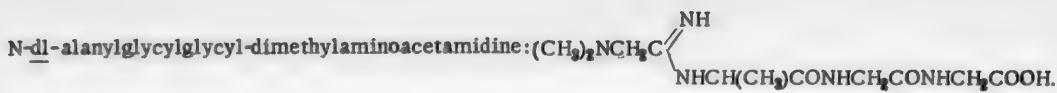
The last compound is of interest because it contains a combination of peptide and amidine linkages. As can be seen from the formulas given, all the above compounds are mono-substituted amidines. Attempts to prepare the corresponding disubstituted compound — N, N'-diphenyl-dimethylaminoacetamidine (in place of N-phenyl-dimethyl-aminoacetamidine) — by using excess aniline and increasing the length of reaction time, lead to formation of the mono-substituted compound without change. Performing the reaction in boiling absolute ether gave the same result. However, aminoimino-ether salts of the β-type — β-dimethylaminopropioiminomethyl ether

$$(CH_3)_2NCH_2CH_2C\!\!\begin{array}{l}\diagup NH\\\diagdown OCH_3\end{array}$$

—readily reacted with aniline to give, depending on the reagent ratio, both mono- and di-substituted amidines:

$$(CH_3)_2NCH_2CH_2C\!\!\begin{array}{l}\diagup NH\\\diagdown NHC_6H_5\end{array}\quad\text{and}\quad (CH_3)_2NCH_2CH_2C\!\!\begin{array}{l}\diagup NC_6H_5\\\diagdown NHC_6H_5.\end{array}$$
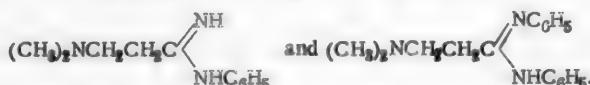
Imino-ethers of amino acids with primary amino groups (for example aminoacetiminomethyl ether and aminoisobutyroiminomethyl ether), have two functional groupings which can react with one another (the amino and the imino-ether groups) to form amidine linkages; this affords the possibility of using these compounds both as the imino-ether and the amino component of the reaction at the same time. In this way unusual amidine poly-condensations may take place:

$$-NH-C(R)_2-C\!\!\begin{array}{l}\diagup NH\\\diagdown NH-C(R)_2-C\!\!\begin{array}{l}\diagup NH\\\diagdown NH-.\end{array}\end{array}$$
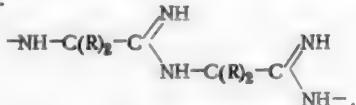
Cyclic compounds may also be formed in this manner. Because the amino acid imino-ethers prepared in our synthesis were separated as dihydrochlorides, it was necessary to remove one molecule of hydrogen chloride from the compound in order to make reactions of the above discussed type feasible; this was accomplished, based on the very different basicity of amino and imino-ether groups, by treating the imino-ether with pyridine. However, use of this reaction on the dihyrochloride of aminoisobutyroiminomethyl ether gave, instead of the desired product, the hydrochloride of aminoisobutyramide:

$$HCl\cdot H_2NC(CH_3)_2C\!\!\begin{array}{l}\diagup O\\\diagdown NH_2\end{array}$$

The similar behavior of several α-substituted imino-ethers which give amides on separation of the free base from the imino-ether salt has been noted in the literature [3]. There are also references to the effect that alcoholysis of imino-ether salts, in which there are two or three substituents on the α-carbon atom, does not lead to orthoesters as is usual, but gives the corresponding amide, for the most part [4].

On treatment of aminoacetiminomethyl ether dihydrochloride with pyridine, we obtained a material whose properties differed both from the corresponding amide and from the initial imino-ether. We were able to conclude that the reaction had gone in the desired direction because of similarity of a number of properties between this compound and N-phenyl-aminoacetamidine (i.e., easy oxidizability in aqueous solution, and ability to give color reactions with certain metallic salts). However, because of the difficulty of purifying the substance prepared, we are not able to make firm conclusions on its structure, for the present.

EXPERIMENTAL

N-Phenyl-dimethylaminoacetamidine-dihydrochloride. 10 ml absolute ether was added to 1 g freshly pre-pared dimethylaminoacetiminomethyl ether dihydrochloride which was ground as finely as possible. A solution of 1 ml aniline in 5 ml absolute ether was then added gradually with cooling. The mixture was allowed to stand at room temperature for a day. From time to time it was shaken and the residue stirred up (with atmospheric moisture ex-cluded). The residue was filtered by suction, washed twice with ether. Yield 1.25 g (96 % of theoretical). The sub-stance was dissolved in a small amount of methyl alcohol, and an equal volume of ether added to the solution. On shaking, the initial turbidity disappeared, and then colorless glistening flakelets began to separate gradually from

the transparent solution. After some time the residue was suction filtered, washed first with an alcohol-ether mixture and then with ether, and dried. Yield 1 g (76% of theoretical).

M.p. 226-227° (with decomp.). A second crystallization of the substance by the above described method gave m.p. 227-228° (with decomp.).

Glistening plates, readily soluble in water and methyl alcohol, less soluble in ethyl alcohol, and insoluble in benzene and ether.

0.1958 g substance: 22.88 ml 0.1 N H_2SO_4 (Kjeldahl). 0.2064 g substance: 24.48 ml 0.1 N H_2SO_4. 0.2008 g substance: 16.2 ml 0.1 N $AgNO_3$ (Volhard). 0.1876 g substance: 15.05 ml 0.1 N $AgNO_3$. Found %: N 16.36, 16.60; Cl 28.6, 28.55. $C_{16}H_{17}N_3Cl_2$. Calculated %: N 16.80; Cl 28.40.

The substance gave a bright blue color with copper salts in aqueous solution in presence of alkali.

N-Phenyl-aminoisobutyramidine-dihydrochloride. 7 ml absolute ether was added to 1.6 g freshly prepared aminoisobutyriminomethyl ether dihydrochloride, 2 ml dry aniline was then added with cooling. The reaction mixture was periodically shaken, and after a day the residue was suction filtered and washed with ether. After drying in a vacuum dessicator we obtained 2 g of material. The latter was treated with a small quantity of ethyl alcohol; most of the material remained undissolved. The mother liquor was removed by suction and discarded (ether separated from the mother liquor a colorless crystalline substance which gave a violet color when treated in aqueous solution with a copper salt and alkali – indicating presence of aminoisobutyramide) and the residue washed with ethyl alcohol, dissolved in methyl alcohol, filtered, and an equal volume of absolute ethyl alcohol added to the solution. In several hours, well-formed crystals separated; these were filtered by suction, washed with ethyl alcohol and ether, and dried in a vacuum dessicator. Yield 1 g. M.p. 246-247°. A mixed melting point test with aminoisobutyramide hydrochloride melted at 230-234°.

The material was readily soluble in water, less soluble in methyl alcohol, and poorly soluble in ethyl alcohol. The aqueous solution of the preparation gave a blue color with copper salts in presence of alkali.

0.1832 g substance: 21.5 ml 0.1 N H_2SO_4. 0.1563 g substance: 18.75 ml 0.1 N H_2SO_4; 0.2100 g substance: 16.9 ml 0.1 N $AgNO_3$. 0.1924 g substance: 15.6 ml 0.1 N $AgNO_3$. Found %: N 16.44, 16.8; Cl 28.56, 28.78. $C_{16}H_{17}N_3Cl_2$. Calculated %: N 16.80; Cl 28.40.

N-Phenyl-aminoacetamidine [(N-phenyl-glycineamidine)-dihydrochloride]. To 1.4 g freshly prepared aminoacetiminomethyl ether dihydrochloride, carefully triturated in 10 ml absolute ether, we added with cooling a solution of 1.5 ml dry aniline in 8 ml ether and allowed the reaction mixture to stand with occasional shaking. A noticeable re-formation of the precipitate took place fairly quickly. After 10 hours the residue was filtered by suction (protected from atmospheric moisture), washed with ether, and dried in a vacuum dessicator. Yield 1.9 g (98% of theoretical). Colorless substance, fairly readily soluble in methyl alcohol. From the solution, ether separated a yellowish oil, which solidified on stirring with ether. After vacuum drying at 60° we obtained an amorphous brownish-white material with a 150-155° melting point range during which it effervesced vigorously and decomposed.

0.1473 g substance: 20.13 ml 0.1 N H_2SO_4. 0.1542 g substance: 20.9 ml 0.1 N H_2SO_4. 0.1038 g substance: 9.35 ml 0.1 N $AgNO_3$. Found %: N 19.13, 18.98; Cl 31.97. $C_8H_{13}N_3Cl_2$. Calculated %: N 18.91; Cl 31.99.

The preparation was readily soluble in water and in methyl alcohol. The solutions quickly became colored on standing, becoming more intense with the passage of time, and a dark precipitate began to separate. The rate of separation of precipitate could be increased by adding sufficient dilute alkali to separate the amidine as a free base. Addition of hydrogen peroxide or passage of air through the solution very considerably accelerated this process.

Aqueous $FeCl_3$ solution gave a blood-red colored solution with N-phenyl-glycine-amidine dihydrochloride, which developed a dirty brown color on standing.

N-Benzyl-dimethylaminoacetamidine-dipicrate. A solution of 2.5 g benzylamide in a small quantity of ether was added with cooling to 1.3 g dimethylaminoacetiminomethyl ether dihydrochloride in 15 ml absolute ether.

After 3 hours the precipitate was suction filtered and washed well with ether. Weight 2.5 g. The material

was dissolved in absolute ethyl alcohol and filtered; to the filtrate we added about one third of its volume of ether. The precipitate which separated was filtered by suction and washed with ether. Weight 0.4 g. M.p. 243-244°. In a mixed melting point test with benzylamine hydrochloride, no depression was obtained.

We then added twice its volume of ether to the filtrate. This precipitate was washed with ether and dried in a vaccum dessicator. Weight 1.4 g. M.p. 155-158°. An abundant yellow precipitate, melting at 219-220°, was obtained on addition of a solution of picric acid in methyl alcohol. When a considerable quantity of ether was added to the previous filtrate an additional 0.4 g of material melting at 156-160° was separated; this substance, like the previous fraction, gave a compound melting at 219-220° with picric acid.

The total yield of N-benzyl-dimethylaminoacetamidine dipicrate was 3.8 g (83% of theoretical). The material was insoluble in water and ether and slightly soluble in methyl and ethyl alcohol.

2.370 mg substance: 0.403 ml N_2 (22°, 795 mm). 2.240 mg substance: 0.386 ml N_2 (22.5°, 796 mm). Found %: N 19.29, 19.53. $C_{23}H_{22}O_{15}N_9$. Calculated %: N 19.41.

N-Phenyl-dimethylaminoacetamidine-dipicrate   We dissolved 1.2 g picric acid in 30 ml absolute methyl alcohol and added 0.7 ml dry aniline. The alcoholic solution was quickly added to 0.6 g freshly prepared dimethyl-aminoacetiminomethyl ether dihydrochloride. The imino-ether salt rapidly dissolved, and in 3-5 minutes a yellow crystalline precipitate of amidine dipicrate began to separate. The precipitate was filtered by suction after 2 hours, and washed twice with methyl alcohol and then with ether. After drying in a vacuum dessicator, the weight of substance was 0.7 g (21% of theoretical). M.p. 217-218° (with decomp.). The substance was insoluble in ether, very slightly soluble in water, and slightly soluble in cold methyl alcohol. In attempts to recrystallize it from hot methyl alcohol, partial decomposition of the substance was observed.

3.938 mg substance: 1.261 mg H_2O. 6.127 mg CO_2. 4.220 mg substance: 1.325 mg H_2O, 6.443 mg CO_2. 2.636 mg substance: 0.449 ml N_2 (16°, 748 mm). 2.206 mg substance: 0.375 ml N_2 (16.5°, 748 mm). Found %: C 41.92, 41.67; H 3.54, 3.51; N 19.80, 19.73. $C_{22}H_{21}O_{14}N_9$. Calculated %: C 41.58; H 3.31; N 19.85.

By treating a solution of N-phenyl-dimethylaminoacetamidine dihyrochloride in methyl alcohol with an alcoholic solution of picric acid, a yellow precipitate rapidly began to separate; this, after washing with alcohol and ether, and drying had m.p. 217-218°. It did not depress the melting point of the N-phenyl-dimethylaminoacetamidine dipicrate prepared above.

N-Glycyl-dimethylaminoacetamidine-dipicrate   We dissolved 0.4 g glycine in 20 ml absolute methyl alcohol which contained 1.5 g picric acid. 0.5 g freshly prepared dimethylaminoacetiminomethyl ether dihydrochloride was added to the solution of glycine picrate; it dissolved very quickly. The transparent solution thus prepared soon began to deposit yellow crystals. The precipitate which formed in an hour was filtered by suction, washed with methyl alcohol, and dried in a vacuum dessicator. Yield 0.6 g (32% of theoretical). M.p. 143-144° (with decomp.). The substance was poorly soluble in most organic solvents.

5.570 mg substance: 0.963 ml N_2 (18°, 755 mm). 5.300 mg substance: 0.920 ml N_2 (18°, 755 mm). Found %: N 20.15, 20.18. $C_{18}H_{18}O_{16}N_9$. Calculated %: N 20.43.

N-dl-Alanylglycylglycyl-dimethylaminoacetamidine-dipicrate. We prepared this, by the procedure of the preceding experiment, from a solution of 0.15 g dl-alanylglycylglycine and 0.5 g picric acid in 10 ml absolute methyl alcohol and 0.5 g dimethylaminoacetiminomethyl ether salt. Yield 0.13 g (20% of theoretical). It had an unsharp melting point of about 120°. It was somewhat soluble in methyl alcohol.

3.685 mg substance: 0.689 ml N_2 (26°, 743 mm). 4.530 mg substance: 0.849 ml N_2 (27°, 743 ml). Found %: N 20.73, 20.90. $C_{29}H_{37}O_{18}N_{11}$. Calculated %: N 20.68.

N-Phenyl-β-dimethylaminopropylamidine-dihydrochloride.   To 1 g freshly prepared β-dimethylamino-propyliminomethyl ether dihydrochloride, suspended in 10 ml absolute ether, was added a solution of 1 ml dry aniline in a small quantity of ether and the mixture allowed to stand for three days with occasional shaking. The precipitate which formed in this period was filtered by suction and washed several times with ether. Yield 1.4 g. The substance was dissolved in hot absolute methyl alcohol, and a small quantity of absolute ether added to the solution after cooling. After a short while it was filtered by suction. 0.1 g ammonium chloride was on the filter. Further addition of dry ether to the filtrate caused the separation of a finely-crystalline material, which was suction filtered and washed with ether. Weight 1 g. After two recrystallizations from absolute ethyl alcohol, we obtained colorless crystals with m.p. 176-177.5°. The material was readily soluble in water and in methyl alcohol and was difficultly soluble in ethyl alcohol.

0.1290 g substance: 14.6 ml 0.1 N. H_2SO_4 (Kjeldahl). 0.1454 g substance: 16.75 ml 0.1 N H_2SO_4. 0.1294 g substance: 9.85 ml 0.1 N. $AgNO_3$ (Volhard). Found %: N 15.85, 16.12; Cl 27.10.. $C_{11}H_{19}N_3Cl_2$. Calculated %: N 15.90; Cl 26.90.

N,N'-Diphenyl-β-dimethylaminopropylamidine-dihyrochloride. A solution of 4 ml aniline in a small quantity of dry ether was added to 2.2 g freshly prepared β-dimethyl-aminopropyliminomethyl ether dihydrochloride triturated in 10 ml absolute ether. The mixture was let stand for two days with occasional shaking. At the end of this time a semi-solid material had settled to the bottom of the reaction vessel. We added double the volume of dry ether (for more complete separation of the substance which, because of high aniline concentration,was partially in solution), and, after a short while, carefully decanted the reaction liquid from the residue. The residue was ground up several times with ether for separation of unreacted amine and then dissolved in a small quantity of absolute ethyl alcohol. Undissolved ammonium chloride was removed by filtration, and an ether solution of hydrogen chloride added to the filtrate until slightly acid. In order to separate the material more completely , we added still more ether, and then, when precipitation was complete, filtered the residue, washed it with ether, and dried it in a vacuum dessicator. Yield 3.5 g. It was twice recrystallized from absolute ethyl alcohol, yielding a colorless crystalline material which was readily soluble in water and methyl alcohol and somewhat less soluble in ethyl alcohol. M.p. 193-194°.

0.1292 g substance: 11.6 ml 0.1 N. H_2SO_4 (Kjeldahl). 0.2014 g substance: 18.25 ml 0.1 N H_2SO_4. 0.2048 g substance: 12.25 ml 0.1N $AgNO_3$ (Volhard). Found %: N 12.56, 12.68. Cl 21.23. $C_{17}H_{23}N_3Cl_2$. Calculated %: N 12.35; Cl 20.89.

Picrate treatment of aminoisobutyroiminomethyl ether dihyrochloride. 15 ml dry pyridine was added with cooling to 3 g aminoisobutyroiminomethyl ether dihydrochloride. The imino-ether salt dissolved amost completely in 15-20 minutes with periodic agitation and a colorless resinous precipitate began to form. After an hour the pyridine was poured off and the residue washed and triturated several times with chloroform and then with ether. The residue was dissolved in methyl alcohol and an excess of ether then added to the solution. A crystalline precipitate separated, which we removed by filtration and washed with ether. After recrystallization from methyl alcohol its m.p. was 264-266° (with decomp.). The material was readily soluble in water and less soluble in methyl and ethyl alcohol. In aqueous solution it formed a violet complex with copper salts and alkali.

3.52 mg substance: 4.485 mg CO_2; 2.559 mg H_2O. 1.955 mg substance: 0.350 ml N_2 (15.5°, 724 mm). Found %: C 34.77; H 8.13; N 20.18. $C_4H_{11}ON_2Cl$. Calculated %: C 34.78; H 7.95, N 20.2.

The prepared material thus appears to have been aminoisobutyramide hydrochloride. The same material is obtained by treatment of the imino-ether salt with the theoretical quantity of pyridine in absolute methyl alcohol.

SUMMARY

1. We prepared a group of N-substituted amino acid amidines, as follows: N-phenylaminoacetamidine, N-phenyl-dimethyl-aminoacetamidine, N-glycyldimethylaminoacetamidine, N-glycylglycyl-dimethylamino-acetamidine, N-dl-alanylglycylglycyl-dimethylaminoacetamidine. The picrates formed readily: in most cases, immediately following mixing the dimethylaminoacetiminomethyl ether salt with the picrate of the corresponding amine in alcoholic solution.

2. We noted the tendency of α-amino acid imino-ethers to yield only the mono-substituted amidine, whereas β-dimethylaminopropyliminomethyl ether on reaction with aniline under analogous conditions readily gave, depending on the reagent ratio, either the mono or the di-substituted amidine.

3. Treatment of aminoisobutyroiminomethyl ether dihydrochloride with pyridine gave aminoisobutyramide hydrochloride. Similar treatment of aminoacetiminomethyl ether dihydrochloride produced a material of undetermined structure.

LITERATURE CITED

[1] N.D. Zelinsky, and N.I. Gavrilov, Moscow State University Transactions (Vestnik), 1947, 57. [2] A. N. Baksheev, J. Gen. Chem. 22, 2025 (1952).* [3] A. Pinner, Die Imidoäther und ihre Derivate. Berlin, pages 31, 37 (1892). [4] S. McElvain, B. Fajardo Pinson, J. Am. Chem. Soc., 67, 690 (1945).

* See Consultants Bureau translation page 2077.

THE SULFONATION REACTION

XXV. SOME PROPERTIES OF NAPHTHALENE TRISULFONYLCHLORIDES

A. A. Spryskov

Of the three naphthalene trisulfonic acids which can be prepared by direct sulfonation, the 1,3,6-trisulfonic has considerable technical value for preparation of H-acid while the 1,3,5-acid has some importance. This, of course, does not mean that the 1,3,7-acid does not have any application. One of the reasons for the insufficiently wide utilization of all the naphthalene trisulfonic acids appears to be the lack of a practical method for separation of the sulfonation mixture into separate isomers because the properties of the trisulfonic acids and their derivatives have been very incompletely studied. Data on solubility of the trisulfonylchlorides in several solvents as well as data on thermal analysis of their mixtures may be of considerable help in investigating mixed naphthalene trisulfonic acids.

We give below results obtained for the solubility in benzene of 1,3,5-, 1,3,6- and 1,3,7-naphthalenetrisulfonylchlorides and the thermal analysis of binary mixtures of the trisulfonylchlorides.

Solubility of Naphthalene-trisulfonylchlorides in benzene
(grams of substance per 100 g solvent)

1,3,5-trichloride		1,3,6-trichloride		1,3,7-trichloride	
at 20°	at 30°	at 20°	at 30°	at 20°	at 30°
14.55	17.50	10.64	14.80	0.86	1.45
14.65	17.54	10.63	14.85	0.86	1.46
14.63		10.87		0.83	1.48

Results of determination of benzene solubility of the trisulfonylchlorides at 20° and 30° are given in the table. The experiments showed that the 1,3,5- isomer was the most readily soluble and that the 1,3,6-isomer was somewhat less soluble. The solubility of the 1,3,7-isomer was substantially different from that of the first two. This difference in solubility allows separation of the 1,3,7-chloride from the 1,3,5- and 1,3,6-chlorides by treatment of the mixture with benzene.
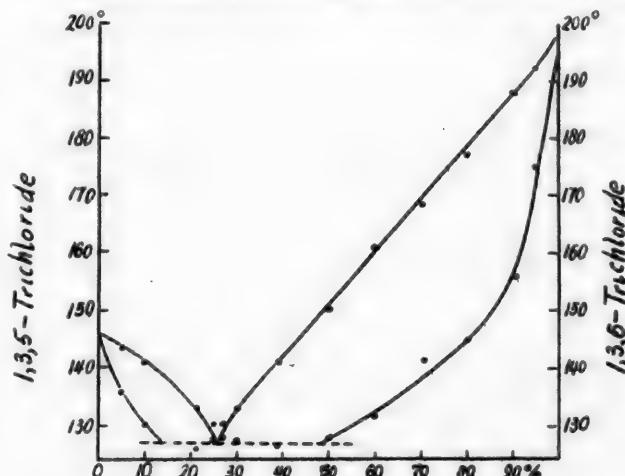
Figure 1.

In complete sulfonation of naphthalene a mixture of only two acids is obtained: 1,3,6-naphthalenetrisulfonic acid and 1,3,5,7-naphthalene-tetrasulfonic acid. This prompted us also to determine the benzene solubility of 1,3,5,7-naphthalene-tetrasulfonylchloride at 20°. The test showed that the tetrachloride was very slightly soluble in benzene. Thus, we found (from the residue after evaporating benzene from a saturated chloride solution) that 100 g benzene dissolved 0.02 g tetrachloride (average of 0.021, 0.023, 0.030). Benzene treatment would thus readily and completely separate the tetrachloride from the 1,3,6-trichloride in products obtained by exhaustive sulfonation.

Results of thermal analysis of binary mixtures of 1,3,5-, 1,3,6- and 1,3,7-trisulfonylchlorides are given in Figures 1, 2, and 3. The results show that the trisulfonylchlorides do not form chemical compounds with each other. The 1,3,5- and 1,3,6-chloride system has a eutectic point at 127°, composition of which corresponds to 74% of the 1,3,5-isomer.

Figure 2.

The 1,3,5- and 1,3,7-isomer system has a 121° eutectic point, corresponding composition 61% 1,3,5-isomer; and the 1,3,6-, 1,3,7- isomer system has a eutectic point of 144° with a corresponding composition of 35% 1,3,6-isomer.

It was shown in one of our papers [1] that 1,7-naphthalene-disulfonylchloride gave, by reaction with chlorsulfonic acid, a mixture of 1,3,5- and 1,3,7-trisulfonylchlorides which melted at 135-144°. Based on these equilibrium thermal diagrams, we may conclude that sulfonation of 1,7-disulfonylchloride yields about 4% 1,3,7- and 96% 1,3,5-trisulfonylchloride.

In sulfonation of 1,3-naphthalene disulfonyl-chloride we obtained a mixture of all three trisulfon-ylchlorides, inasmuch as the sulfonation product melted at a temperature below the eutectic point of any of the binary mixtures.

EXPERIMENTAL

For the tests we used 1,3,5-naphthalene-trisulfonylchloride with m.p. 146°, 1,3,6-chloride with m.p. 198°, and 1,3,7- chloride with m.p. 165.5°, and benzene with a 5° solidification temperature.

Figure 3.

Solubility determinations were made in a Pavlevsky apparatus [2], supplemented by a stirrer in the saturated solution container. The entire apparatus was mounted in a thermostat, the temperature of which was held with 0.1° of the values given in the table. Each run lasted 1.5 to 7 hours, with stirring.

The data for the thermal equilibrium diagrams were obtained in the following manner. The mixture of isomers was dissolved in benzene and the solvent evaporated. The residue was placed in a capillary and heated in an apparatus for melting point determination. The temperatures at which the first trace of liquid appeared and at which the last trace of crystals disappeared were observed. Heating took place sufficiently slowly that the temperature rose 1° in about 5 minutes, and the determination was repeated 3 or more times.

P. T. Pestov collaborated in this work.

SUMMARY

1. The solubility of 1,3,5-, 1,3,6-, and 1,3,7-naphthalene-trisulfonylchloride and of 1,3,5,7-naphthalene-tetrasulfonylchloride in benzene at 20° and 30° has been determined.

2. Thermal equilibrium diagrams have been prepared for the binary systems: 1,3,5- and 1,3,6-trichloride, 1,3,5- and 1,3,7-trichloride, and 1,3,6- and 1,3,7-trichloride.

LITERATURE CITED

[1] A. A. Spryskov, J. Gen. Chem., 22, 661 (1952). *
[2] Br. Pawlewski, Ber., 32, 1040 (1899).

* See Consultants Bureau translation page 727.

3-ETHYLIMIDOSULFAMIDE AND ETHYLSULFAMIDE

A. V. Kirsanov and Yu. M. Zolotov

3-Ethylimidosulfamide was prepared with a 20.4% of theoretical yield by action of ethyl iodide on the silver salt of imidosulfamide. The very same ethylimidosulfamide was also prepared by reaction of diazoethane on free imidosulfamide with a yield which was 86.3% of the theoretical quantity. The formation of ethylimidosulfamide by this procedure shows, as does neutrality of its freshly prepared aqueous solution, that a hydrogen atom of the ethyl group is replaced by a middle nitrogen atom.

Thus, as does 3-methylimidosulfamide [1], 3-ethylimidosulfamide readily hydrolyzes completely with formation of sulfamic acid and ethylsulfamide.

EXPERIMENTAL

Ethylation of silver salt of imidosulfamide by ethyl iodide. Preliminary experiments showed that when a mixture of imidosulfamide silver salt stands at room temperature with excess ethyl iodide, almost exactly one molecule of ethyl iodide enters the reaction, although only 20.4% ethylimidosulfamide is thus formed. The rest of the ethyl iodide is used up, evidently by formation of polyethylated imidosulfamide from the reaction products. Consequently 39.9% of the imidosulfamide reacted with 79.6% of the ethyl iodide. It therefore follows that the polyethylated products are mainly diethylimidosulfamide. Actually, the yield of noncrystalline oily reaction product is in good agreement with these calculations. One of these experiments is described.

A mixture of 0.01 mole crushed anhydrous silver salt of imidosulfamide (2.82 g) and 3.0 ml ethyl idodide was allowed to stand for four days at room temperature in the dark. During this time the colorless silver salt of imidosulfamide was converted into light green silver iodide. Excess ethyl iodide was vaporized under vacuum at 40°. The reaction mixture weighed 4.36 g after this; consequently 1.54 g ethyl iodide reacted, i.e., 98.7% of the theoretical quantity. The dry mass was extracted twice by (125 ml) boiling benzene. From the first portion, 0.31 g 3-ethylimidosulfamide crystallized on cooling as snow-white, fine, matted needles. The product was filtered by suction and washed with benzene. Nothing separated from the second portion. The mother liquor and second portion were combined and concentrated on a water bath to a 25 ml volume. After a day, an additional 0.10 g of matted needles separated. Total yield of 3-ethylimidosulfamide was 0.41 g, i.e., 20.4% of the theoretical quantity.

The mother liquor was evaporated to dryness at 60° under vacuum. 0.82 g of an oily noncrystalline product was obtained as a residue. If we regard this material as mainly composed of diethylimidosulfamides, the yield of this corresponds to 35.4% of theoretical.

The residue after extraction of ethylated products by boiling benzene appeared to be a mixture of silver iodide and free imidosulfamide. In order to separate the latter mixture, we extracted it four times with 15.0 ml portions of ethyl acetate. We added some activated carbon to the turbid extract; after filtration the colorless, transparent filtrate was evaporated to dryness at 40° under vacuum. In order to remove the small quantity of ethylated imidosulfamides present in the crystalline residue, it was washed twice with 50 ml portions of boiling benzene and then dried under vacuum. The yield of free imidosulfamide was 0.69 g, i.e., 39.7% of the theoretical quantity; m.p. 154-158°. After recrystallization from acetone with benzene it gave fine needles, m.p. 163-165°.

Thus, overall reaction balance is: free imidosulfamide 39.7%, 3-ethylimidosulfamide 20.4%, oily products (considered as diethylimidosulfamides) 35.4%. Sum, 95.5% of theoretical. This agreement confirms the assumption that the oily product mainly consists of diethylimidosulfamides.

3-Ethylimidosulfamide was a colorless crystalline material, readily soluble in water, alcohol, acetone, ether, and ethyl acetate; it was very difficulty soluble in cold benzene —somewhat better in boiling benzene. Small quantities of 3-ethylimidosulfamide can be conveniently crystallized from benzene, larger quantities —from a mixture

of ether and benzene. When recrystallized from benzene, 3-ethylimidosulfamide gave fine matted needles. When heated in a capillary, 3-ethylimidosulfamide melted without decomposition at 113-115°, i.e., almost the same as 3-methylimidosulfamide (113-114°).

A freshly prepared aqueous solution of 3-ethylimidosulfamide was neutral to Congo red and had a weak bitterish taste; however, even in a few minutes at room temperature the reaction to Congo red became acid and it developed an intensely acid taste, which indicates how quickly hydrolysis occurred.

0.0414 g substance: 0.0178 g CO_2; 0.0162 g H_2O. 0.0608 g substance. 0.0263 g CO_2; 0.0250 g H_2O. Found %: C 11.73, 11.80; H 4.36, 4.60. $C_2H_8O_4N_3S_2$. Calculated %: C 11.83; H 4.46.

Ethylation of free imidosulfamide with diazoethane. To a mixture of 0.02 mole crushed imidosulfamide (3.5 g) in 75 ml absolute ether at a temperature of about 10°, we added in small portions while vigorously stirring by hand, about 0.02 mole diazoethane as an approximately 0.2 N ether solution. After each addition the mixture began to turn yellow, and then decolorized with liberation of nitrogen. The imidosulfamide gradually went into solution. We stopped adding the diazoethane solution when the yellow color lasted for more than one minute.

0.5 g dry activated carbon was added to the turbid ether solution, and filtered. The entire colorless transparent solution was concentrated on a water bath to a volume of about 40 ml during which it began to crystallize. 200 ml absolute benzene was added to the warm solution, while stirring smoothly, and it was allowed to crystallize for 3-4 hours.

The precipitated 3-ethylimidosulfamide was filtered by suction, washed with benzene, and dried in a vacuum dessicator. Yield 2.63 g, m.p. 108-110°. The mother liquor was evaporated to a 50 ml volume, and the crystals which separated suction filtered and washed with benzene; yield 0.39 g, m.p. 111-113°. Total yield 3.02 g, i.e., 86.3% of the theoretical quantity.

For purification, the 3-ethylimidosulfamide was either dissolved in ether and precipitated by addition of five volumes of benzene, or it was recrystallized from a large volume of boiling benzene. Pure 3-ethylimidosulfamide melted at 113-115° (uncorr.) without decomposition and did not depress the melting point of 3-ethylimidosulfamide prepared from imidosulfamide silver salt and ethyl iodide.

Saponification of 3-ethylimidosulfamide. Preparation of ethylsulfamide. 2.63 g 3-ethylimidosulfamide was added to 10.0 ml water; the solution was quickly brought to a boil, cooled, and evaporated to dryness under vacuum on a water bath heated to 25°. The dry residue was extracted with acetone and the acetone solution evaporated to dryness under vacuum. The residue was ethylsulfamide in the form of a colorless oil, which when cooled and vigorously rubbed with a glass rod began to crystallize. Yield of ethylsulfamide was 1.31 g, i.e., 81.4% of the theoretical quantity. For purification, the product was extracted by boiling benzene. Combined benzene solutions were concentrated under vacuum to 25 ml, and this solution allowed to crystallize at 10° Within a day, fine needles separated which were similar to glass wool; they were suction filtered, washed with benzene, and dried under vacuum. Yield 0.85 g, m.p. 30-32° (uncorr.). For further purification, the product was dissolved in 1.5 ml acetone and 15 ml benzene added to the solution. The crystals which separated were washed with benzene and dried. Yield 0.63 g, m.p. 33-35°. Melting point was not increased by subsequent recrystallization.

Ethylsulfamide was a colorless crystalline material, readily soluble in water, ethyl acetate, and acetone. It dissolved with difficulty in cold benzene, somewhat better in hot. Aqueous solutions of ethylsulfamide were neutral. Ethylsulfamide crystallized from benzene as fine needles, similar to glass wool. On evaporation of solutions in ethyl acetate, ethylsulfamide separated as short prisms. Pure ethylsulfamide melts without decomposition at 33-35° (uncorr.).

0.0057 g substance: 1.088 ml N_2 (15°, 755 mm). Found %: N 22.47. $C_2H_8O_2N_2S$. Calculated %: N 22.57.

SUMMARY

3-Ethylimidosulfamide was made both by action of ethyl iodide on imidosulfamide silver salt and by action of diazoethane on free imidosulfamide. Its properties have been described. By hydrolysis of 3-ethylimidosulfamide we prepared ethylsulfamide and reported its properties.

LITERATURE CITED

[1] A.V. Kirsanov and Yu. M. Zolotov, J. Gen. Chem., 21, 642 (1951). *

ALKYLATION OF AMINES BY DIALKYLPHOSPHORYL CHLORIDES

B. P. Lugovkin and B. A. Arbuzov

As a development of our work [1] on synthesis of ethyl phosphonic acid esters containing heterocyclic radicals, we studied the reaction of diethyl- and dibutylphosphoryl chlorides on carbazole trying to prepare esters of N-phosphono-carbazole.

Experiments with diethylphosphoryl chloride and carbazole in benzene and toluene media did not give positive results. Despite heating for many hours, the carbazole remained unchanged.

When carbazole and diethylphosphoryl chloride were heated without solvent at a temperature of 210°, a vigorous reaction took place with evolution of ethyl chloride and hydrogen chloride. The reaction results were somewhat unexpected. N-ethylcarbazole was separated to the extent of 25%. In the case of reaction with dibutyl-phosphoryl chloride, N-butylcarbazole, in the amount of 29%, was separated.

Having come upon this interesting case of alkylation by dialkylphosphoryl chlorides, we extended the study to include reaction of dialkylphosphoryl chlorides with other materials containing primary and secondary amino groups. When diphenylamine was heated with dimethylphosphoryl or diethylphosphoryl chlorides a violent reaction occurred; the corresponding alkyl halide and hydrogen chloride were liberated, and N-methyldiphenylamine (yield 69% of theoretical) or N-ethyldiphenylamine (yield 83% of theoretical) was formed.

The large yields of N-substituted diphenylamines gives this reaction interest from the point of view of synthesis, because other methods for preparing alkyldiphenylamines do not give high yields (with diethyl sulfate the yield of N-ethyldiphenylamine is 39% [2]). The acid chlorides of dialkylphosphoric acids are available, nowadays, in view of the method for their preparation by chlorination of dialkylphosphoric acids.

Of the amines with primary amino groups we took aniline and β-naphthylamine. The reaction with aniline took place in two stages. The first stage occurred during heating to 110-125° and was associated with liberation of the alkyl (ethyl) chloride and hydrogen chloride. The second stage took place at 190° and was accompanied by evolution of considerable heat. As a result of the action of excess diethylphosphoryl chloride we obtained diethylaniline with a yield 87% of theoretical.

The reaction of diethylphosphoryl chloride on β-naphthylamine proceeded similarly. As a result we obtained N-diethyl-β-naphthylamine with a yield 88% of theoretical. Unheated α-aminopyridine and dimethyl-phosphoryl chloride reacted violently and resulted in a temperature rise to 230°. N-methyl-pyridone-imine was separated from the reaction products in a 29% of theoretical yield.

In order to examine the nature of the reaction of dialkylphosphoryl chlorides on amides, we performed an experiment on the action of dimethylphosphoryl chloride on benzamide. As a result of this experiment, we separated N-methylbenzamide to the extent of 34% of the theoretical yield.

The alkylation reaction using organic derivatives of phosphoric acid does not appear new. Completely esterified phosphoric acid, in the presence of alcoholates, alkylates alcohols [3] and phenols [4]. Alkylation of amines by completely esterified phosphoric acid has been described. Billman, Radike, and Mundy [5] alkylated aniline and α- and β-naphthylamines using fully esterified phosphoric acid and prepared the corresponding

dialkylarylamines in good yield according to the equation:

$$3Ar-NH_2 + 2(RO)_3PO \longrightarrow 3Ar-N(R)_2 + 2H_3PO_4.$$

Rueggerberg and Chernack [3] prepared N-ethylmorpholine from morpholine and triethyl phosphate. Rueggerberg and Chernack assume the formation of ammonium salts in reaction of an amine with phosphoric acid esters. The latter, under the action of alkali, alkylates the amine.
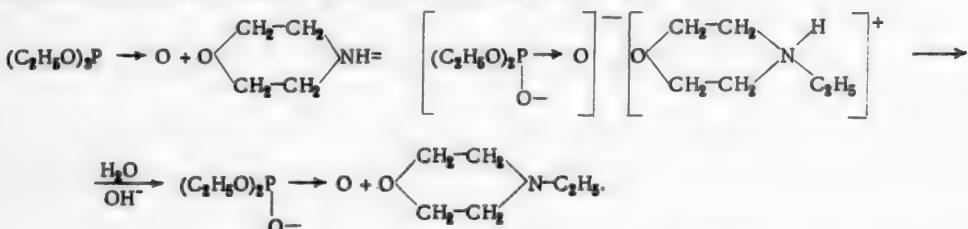
Formation of ammonium salts as intermediate products is also assumed by Todd, Baddiley, Clark, and Michalski [6] for the reaction of dibenzylphosphoryl chloride on tertiary amines. The ammonium salt decomposes according to the scheme:
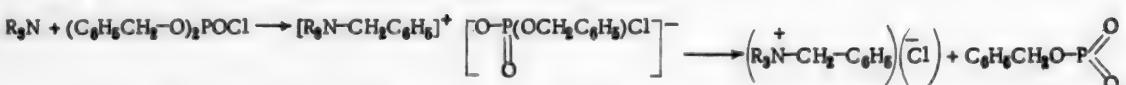
As far as the mechanism of amine alkylation by reaction with dialkylphosphoryl chloride is concerned, although it is given in the present paper, we do not regard it as explained.

A. E. Arbuzov and B. P. Lugovkin [7], and McCombie, Saunders, and Stacey [8] have shown that the acid chlorides of dialkylphosphoric acids react with aniline to form diethylphosphoric acid anilides and aniline hydrochloride. Evidently, these products must form first before the reaction described in the present paper.

In order to investigate the possibility of forming alkylated amines from dialkylphosphoric acid anilides on heating, we performed a test in which we heated the anilide of diethylphosphoric acid. When heated to 230° a violent reaction took place, and the liquid separated into two layers. On cooling the upper layer was an oily liquid while the lower layer was a solid glassy material. Treatment of the solid material with alkali gave an additional quantity of the oily product. This oily material was shown to be diethylaniline. Yield 85.2% of theoretical. Heating diethylphosphoric acid anilide in presence of 2 moles of aniline hydrochloride leads to formation of ethylaniline.

It thus seems that amine alkylation, in the given cases, takes place via thermal decomposition of initially formed anilides.

With regard to the manner of formation of diethylaniline from the anilide, we propose the following, preliminary scheme:
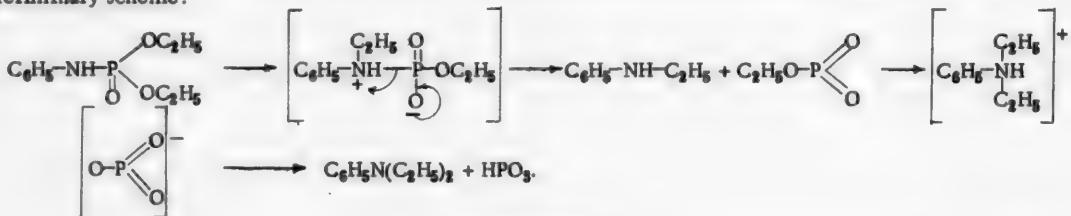
EXPERIMENTAL

Reaction of diethylphosphoryl chloride and carbazole. Test I. To 10 g carbazole in 40 ml dry benzene we added 18.2 g diethylphosphoryl chloride (b.p. 82° at 11 mm, n_D^{18} 1.4169, d_{20}^{20} 1.1953 [9]). This was heated at the boiling point of benzene for 6 hours. After distillation of benzene, we recovered the starting materials, as follows: 8.3 g carbazole (m.p. 238°, mixture test 238°) and 9.7 g acid chloride (b.p. 77° at 7 mm, n_D^{20} 1.4185, d_{20}^{20} 1.1937.

Test II. A mixture of 9.7 g carbazole, 12.8 g acid chloride, 10 g freshly distilled dimethylaniline, and 40 ml dry toluene was heated at the temperature of boiling toluene for 6 hours. After an hour of heating the

reaction mixture separated into two layers. We extracted from the toluene solution 1 g carbazole and 3 g dimethylaniline (b.p. 61-62° at 5 mm, n_D^{20} 1.5442, d_{20}^{20} 0.9630). By treating the lower layer with water we separated 8.3 g unchanged carbazole, i.e., a total of 9.3 g carbazole recovered (m.p. 237-238°, mixture test 237-238°). On alkalization with NaOH, 5 g dimethylaniline was separated.

Test III. 9 g acid chloride was added to 6.8 g carbazole. On heating (in a Claissen flask) on a Wood's metal bath, a violent reaction took place with separation of C_2H_5Cl and HCl; the temperature rose to 210°. The reaction product was dissolved in absolute alcohol with boiling. Extended cooling (to minus 10°, on the average) partially separated the unchanged carbazole. The recovered carbazole weighed 1.2 g (m.p. 234°). After distillation of the alcohol, the residue, which was a thick liquid, was vacuum distilled at 5 mm and 167-169°. An oily liquid (3.8 g) was distilled which crystallized on cooling. After recrystallization from alcohol we obtained 2 g (25%) N-ethyl-carbazole. The picrate, recrystallized from alcohol, formed dark-red-colored small needles which melted at 97-98°. A mixture test with synthetic N-ethylcarbazole (m.p. 100°) melted at 100-101°. The N-ethyl-carbazole (m.p. 100°) melted at 100-101°. The N-ethylcarbazole separated by decomposing the picrate by an aqueous solution of ammonia melted at 68-69° (mixture test).

Reaction of di-n-butylphosphoryl chloride on carbazole. We added to 6 g carbazole 8.4 g di-n-butyl phosphate acid chloride (b.p. 117° at 8 mm, n_D^{19} 1.4310, d_{20}^{20} 1.0824 [10]). At a temperature of 170-175° a reaction took place with release of hydrogen chloride which lasted for 15 minutes. We added an additional 5.3 g acid chloride to the residue. Heating was continued at 135-140° for 45 minutes. On distillation under a 3 mm vacuum a crystalline and oily product (7.3 g) distilled at 200-208°. The tarry residue (5.4 g) was not investigated. The distilled material was dissolved in absolute alcohol and on extensive cooling (on the average to minus 10°) unchanged carbazole partially separated (2.8 g, m.p. of picrate 179-181°; mixture test 180°; lit. values 182°, 186°). Following distillation of the alcohol, the thick liquid was again distilled under 5 mm vacuum at 210-218°. We distilled 2.3 g or 28.7%. N-n-butylcarbazole, which was completely converted to the picrate in alcoholic solution. The picrate formed ruby-red long needles melting at 88° (following recrystallization from alcohol). A mixture test with the picrate of synthetic N-n-butylcarbazole (m.p. 89°) melted at 89°.

Heating tests on diethylphosphoryl and dimethylphosphoryl chlorides. 12 g diethylphosphate acid chloride was heated on a Wood's metal bath. At a temperature (in the flask) of 150-160° a vigorous release of ethyl chloride (burning with a green color) and hydrogen chloride (NH_4Cl) took place. The gaseous products weakly decolorized bromine water ($CH_2=CH_2$). Unchanged acid chloride was not observed after an hour of heating. The residue, which was a colorless syrupy liquid, was not investigated. Decomposition of the acid chloride of dimethyl phosphate (b.p. 64-65° at 10 mm, n_D^{20} 1.4118, d_{20}^{20} 1.3455 [11]) took place at 100° with mild release of methyl chloride and hydrogen chloride. At temperatures of 140-145°, vigorous liberation of methyl chloride and hydrogen chloride occurred, during which bromine water was weakly decolorized. The residue was also a syrupy liquid.

Reaction of diethylphosphate acid chloride with diphenylamine. On heating 8.3 g diphenylamine (dried at 120°) with 12.2 acid chloride at 140-155° a violent reaction took place with release of ethyl chloride and hydrogen chloride. The mixture was heated at 155-165° for 45 minutes (until evolution of gaseous products ceased). Two phases were formed: the upper was an oily liquid and the lower a syrup which solidified on cooling. After separation of the upper layer, the residue was treated with a concentrated soda solution; the oily liquid which formed was combined with the main product. An ether extract was prepared which was dried with sodium sulfate.

N-Ethyldiphenylamine was vacuum distilled at 147-148° (11-12 mm) as a colorless oily liquid; n_D^{20} 1.6085, d_{20}^{20} 1.0386. Yield 8 g, 82.7% of theoretical. N-Ethyldiphenylamine on redistillation at 147° (10 mm) gave n_D^{20} 1.6095, d_{20}^{20} 1.0396.

To 1 g N-ethyldiphenylamine (once distilled), dissolved in 5 ml dry chloroform, we added 1.6 g bromine in 5 ml dry chloroform dropwise with cooling (in snow). The mixture was treated with a concentrated soda solution, dried with calcium chloride, and the chloroform evaporated. By recrystallization from a mixture of benzene and petroleum ether, we obtained 1.6 g (theoretical quantity is 1.8 g) N-ethyldiphenylamine dibromide melting at 107-108°.

0.1106 g substance: 0.1160 g AgBr(Carius.) Found %: Br 44.63. $C_{14}H_{13}NBr_2$. Calculated %: Br 45.04.

* Temperatures in all of the tests were measured in the reaction mixture.

Literature constants for N-ethyldiphenylamine are: b.p. 149-150° at 10 mm, dibromide (p,p'-) m.p. 107-108° [12].

Reaction of dimethylphosphoryl chloride with diphenylamine. On heating 9 g diphenylamine and 11.5 g acid chloride to a temperature of 110-115°, methyl chloride and hydrogen chloride were liberated. At 120-125° a violent reaction occurred which raised the temperature to 170° (without heat). The resulting product was worked up in the same way as in the diethylphosphate experiment. N-Methyldiphenylamine was distilled at 153-155° (15-16 mm) as a colorless oily liquid; n_D^{20} 1.6238; d_{20}^{20} 1.0596; yield 6.7 g or 68.8% of theoretical. On redistillation, b.p. was 147-148° at 11 mm, n_D^{20} 1.6230, d_{20}^{20} 1.0572. We prepared N-methyldiphenylamine dibromide (under the same conditions as for N-ethyldiphenylamine); colorless small needles melting at 119° (after recrystallizing twice from alcohol).

Literature constants for N-methyldiphenylamine are: b.p. 145-146° at 10 mm, 148° at 13 mm, dibromide (p,p'-) m.p. 120° [12].

Reaction of diethylphosphoryl chloride and aniline. We added 37 g acid chloride to 10 g aniline (freshly distilled), during this the temperature rose to 95° with release of ethyl chloride and hydrogen chloride. When heated to 110-125° it frothed vigorously and released considerable ethyl chloride and a small amount of hydrogen chloride. It was heated for 15 minutes (until evolution of gaseous products ceased). The mix was cooled to 110° and an additional 18.5 g acid chloride added. It was again heated to 110-120° for 15 minutes and then to 160-170° for 15 minutes; on continuing the heating to 190° a violent reaction ensued which raised the temperature to 230° (without further heating); liberation of gaseous materials stopped. The glassy-appearing reaction product was dissolved in 30 ml water with heating; on cooling, the solution was neutralized, using a concentrated solution of potassium hydroxide. The oily liquid which formed was separated, and the water solution extracted with ether; both were dried with potassium hydroxide. The reaction product distilled at 91-94° (10 mm) as a colorless oily liquid; n_D^{20} 1.5410, n_D^{22} 1.5400, d_{20}^{20} 0.9407. The picrate which formed yellowish-green colored crystals melting at 137-138° melted at 138-139° after recrystallization from alcohol. A mixture test with the picrate of N-monoethylaniline (yellow color, m.p. 136-136.5°) gave a depressed melting point (110-115°).

The distillation gave 14 g diethylaniline, or 87.5% of theoretical. On redistillation (12.7 g) diethylaniline was obtained in the following fractions at 10 mm:

I. 88-89°, n_D^{20} 1.5440, n_D^{22} 1.5435, d_{20}^{20} 0.9518 (1.8 g); picrate had a yellow-green color with m.p. 138-139°.

II. 89-90°, n_D^{20} 1.5410, n_D^{22} 1.5400, d_{20}^{20} 0.9402 (10.1 g); picrate had a yellow-green color with m.p. 138-139°.

Picrates of the I and II fractions had a depressed melting point (110-115°) when melted with the picrate of monoethylaniline (m.p. 136-136.5°).

Literature constants are [13]: aniline; b.p. 69° at 10 mm, n_D^{22} 1.5848, d_{20}^{20} 1.0219; picrate light yellow in color, m.p. 181°; monoethylaniline: b.p. 84° at 10 mm, 206° at 760 mm, d_{15}^{18} 0.9705, n_D^{20} 1.5559; picrate, yellow in color, m.p. 132°; diethylaniline: b.p. 215-216°, 92° at 10 mm, n_D^{22} 1.5410, d_{15}^{18} 0.9350; picrate, yellowish green color, m.p. 142° and 135-136°.

Reaction of diethylphosphoryl chloride on β-naphthylamine. 24 g acid chloride was added to 10 g β-naphthylamine (dried at 110°); the temperature rose to 50°. On heating to 120° vigorous frothing and evolution of ethyl chloride and hydrogen chloride took place. The temperature was held to 120-130° for 15 minutes (until frothing became weak). On heating to 180-185° a violent reaction (with release of ethyl chloride together with mild evolution of hydrogen chloride) took place; the temperature rose (without further heating) to 260°. The reaction mixture was a very thick liquid. The mixture was cooled to 65° and an additional 24 g acid chloride added. The reaction was then carried out for 15 minutes at 120-130° and for 40 minutes at 175-185° (until evolution of gaseous products became weak). After working up (see the experiment with aniline) the product gave on vacuum distillation at 10 mm the following fractions:

I. 167-168°; light yellow-colored liquid with blue fluorescence, n_D^{20} 1.6270, 1.4 g.

II. 169-172°; light yellow-colored liquid with blue fluorescence, n_D^{20} 1.6335, d_{20}^{20} 1.0215. 12.2 g N-diethylnaphthylamine was distilled, or 87.7% of theoretical. The picrate formed yellow colored crystals which melted at 151-152°. The melting point did not change on recrystallization from alcohol.

We prepared the hydrochloride of N-diethyl-β-naphthylamine (by passing dry hydrogen chloride through a dry ether solution); it melted at 169-170°. After recrystallization from a mixture of chloroform and dry benzene it melted at 175°.

0.0932 g substance: 0.0574 g AgCl. Found%: Cl 15.23. $C_{14}H_{17}N \cdot HCl$. Calculated %: Cl 15.06.

Literature constants [14] are: β-naphthylamine, b.p. 306°; N-monoethylnaphthylamine, b.p. 315-316°; 167° at 10 mm; N-diethylnaphthylamine, b.p. 316°; hydrochloride, m.p. 175° or 177-178°.

Reaction of dimethylphosphoryl chloride on a-aminopyridine. 16 g acid chloride was added to 10 g a-aminopyridine (dried at 110°); a very violent reaction ensued with liberation of methyl chloride and mild evolution of hydrogen chloride, the temperature rose from 20° to 230°. The mixture was cooled to 95° and 16 g additional acid chloride added. It was heated at 95-120° for 15 minutes with violent release of methyl chloride and mild evolution of hydrogen chloride. The glassy reaction product was dissolved in 60 ml water with heating, and on cooling was neutralized by water and then by potassium hydroxide. It was extracted (with thorough stirring of the pasty mass) using several portions of ether (total volume 130 ml). After drying over potassium hydroxide and distillation of the ether an oily reddish-brown liquid was obtained; the latter was distilled with negligible residue (b.p. 107-110° at 18 mm, yellow colored liquid, yield 3.3 g or 28.7% of N-methylpyridone-imine).

2.5 g of the fraction was dissolved in 10 ml alcohol and 3.5 g picric acid added, a yellow colored picrate precipitated at once. 4.4 g of picrate were separated, m.p. 170-180°. After recrystallization from alcohol (130 ml) the melting point was 197-198°, 3 g. A second recrystallization from alcohol gave m.p. 199-200°, yellowish green in color. A mixture test with the picrate of synthetic N-methylpyridone-imine (m.p. 199-200°) melted without depression at 199-200°. From the mother liquor (of the picrate preparation) we obtained a yellow colored picrate having m.p. 158-167° (0.7 g). In view of its small quantity, this picrate was not identified. The orange colored picrate of methyl-a-aminopyridine was not observed. Also unobserved was the picrate of unchanged a-aminopyridine.

Literature values [15]: methyl-a-aminopyridine: b.p. 100-102° at 18 mm; orange colored picrate, m.p. 190° or 193-194°; N-methylpyridone-imine: b.p. 108° at 16 mm; yellowish green colored picrate, m.p. 199-201°; dimethyl-a-aminopyridine: b.p. 196°; yellow colored picrate, m.p. 182°; N-methylpyridonemethylimine: b.p. 128° at 38 mm; yellow colored picrate, m.p. 160°.

Reaction of dimethylphosphoryl chloride on benzamide. 14.5 g acid chloride was added to 6 g benzamide (dried at 120°). A violent reaction occurred on heating to 80° with release of methyl chloride and hydrogen chloride; the temperature rose to 120° without further heating. When the reaction was finished, in about 15 minutes, we added an additional 10 g acid chloride. After 15 minutes of heating at 120-140°, heating was continued at 170-180° (for 5 minutes until evolution of gaseous products ceased). The reaction product was treated with a concentrated solution of potassium hydroxide and the oily liquid layer which formed separated using benzene extraction; the extract was dried over sodium sulfate. The benzene was vaporized and the reaction product then distilled under vacuum as follows:

Fraction I: 88-170° at 15 mm (most of it at 88°); colorless liquid 0.8 g .

Fraction II: 174-178° at 15 mm; very thick liquid, partially crystallized, 4.5 g. The crystalline product was filtered after cooling. We obtained 1.5 g N-methylbenzamide with m.p. 71-73°. Following crystallization from aqueous alcohol its m.p. was 79-80°. The oily liquid product was redistilled, and it came over completely at 175-177° (16 mm) as a thick liquid. The crystals which formed on slow cooling were pressed on a clay plate; we obtained an additional 0.8 g N-methylbenzamide with m.p. 75-77°. A mixture test with benzamide melted with depression at 62°. The total yield of N-methylbenzamide was 2.3 g, or 34.4% of theoretical.

Literature constants [16]: N-methylbenzamide, b.p. 167° at 11 mm, m.p. 75, 78 and 82°; N-dimethyl-benzamide, b.p. 132° at 15 mm, m.p. 41-42°.

Experiment on heating diethylphosphoric acid anilide with aniline hydrochloride. 10.9 g diethylphosphate anilide (m.p. 95-96°) • and 12.8 g (2 moles) aniline hydrochloride were heated on a Wood's metal bath. At a temperature of 100-110° (in the flask) ethyl chloride was energetically evolved with frothing. After 5 minutes

_____

• Diethylphosphate anilide was prepared by the Arbusov-Lugovkin method (see [7]). 20 g acid chloride was added to 21.2 g aniline (freshly distilled). The temperature rose to 144°. We obtained 15.6 g (59.6%) anilide and 10.9 g (73.7%) aniline hydrochloride.

the temperature was increased by heating to 145-156° over a 15 minute period with vigorous release of ethyl chloride. On heating to 200-225° the ethyl chloride evolution (which resulted in effervescence of the reaction mixture) stopped. Evolution of hydrogen chloride did not occur. After suitable working up (see experiment with aniline) and a second vacuum distillation at 10 mm, we separated the following fractions:

I. 72-75°; oily liquid smelling like aniline, n_D^{20} 1.5785, n_D^{22} 1.5779, d_{16}^{20} 1.0040; light yellow color picrate, m.p. 181-182° (from ether); after recrystallization from alcohol its m.p. was 184-185°; mixture test with aniline picrate melted without depression; 5.7 g aniline distilled.

II. 75-77°; n_D^{20} 1.5728, d_{16}^{22} 0.9949 (2.1 g); the picrate was the same as for fraction I; total aniline distilled was 7.8 g (according to the theory 8.83 g should be obtained from the aniline hydrochloride), or 88.3%.

III. 80-82°; colorless oily liquid (with weak blue fluorescence) n_D^{20} 1.5640, n_D^{22} 1.5630, d_{16}^{20} 0.9771; yellow colored crystalline picrate with m.p. 136-136.5° (from ether); after two recrystallizations from alcohol the melting point was unchanged. A mixture test with the picrate of diethylaniline (m.p. 138-139°) melted with depression (110-115). 5.7 g monoethylaniline was distilled (99.0%).

Literature constants: refer to experiment with aniline.

Test on heating the anilide of diethylphosphoric acid. 8.1 g diethylphosphate anilide (m.p. 95-96°) was heated at a temperature of 120-130° for 30 minutes; at 160-170° for 15 minutes (it was somewhat violent), and when heated to 230° a violent reaction took place with effervescence and separation into two layers; the temperature rose (without further heating) to 240°. The material was rapidly cooled to 200° and again heated to 240°. On cooling, the upper layer was an oily liquid insoluble in water with a diethylaniline odor; the lower layer, a glassy solid material, was worked up in a concentrated solution of potassium hydroxide, the oily liquid which separated was combined with the upper layer, the residue was extracted with ether, and the extract dried over KOH. The reaction product completely distilled at 86-87° (10 mm) as an oily liquid. On redistillation its b.p. was 86° at 10 mm, n_D^{20} 1.5434, n_D^{22} 1.5420, d_{16}^{20} 0.9387. Yellowish-green crystalline picrate (from ether) had m.p. 138-139° (after two recrystallizations from alcohol). A mixture test with the picrate of diethylaniline (experiment with aniline) melted at 139-140°. 4.5 g diethylaniline was distilled (85.2%).

Literature constants: see the aniline experiment.

SUMMARY

1. We studied the reaction of diethylphosphoryl chloride and dibutylphosphoryl chloride on carbazole. It was shown that reaction takes place when the components are heated above 200°, and that as a result N-ethyl- and N-butyl-carbazole are obtained, respectively.

2. The alkylating effect of dialkylphosphoryl chlorides has been stated with regard to aniline, β-naphthyl-amine, diphenylamine, and a-aminopyridines. As a result of these reactions, we obtained N-diethylaniline (87%), N-diethyl-β-naphthylamine (88%), N-ethyldiphenylamine (83%), N-methyldiphenylamine (69%), and N-methyl-pyridoneimine (29%), respectively.

3. Alkylation by dialkylphosphoryl chlorides takes place even in the case of amides, as has been shown using benzamide as an example.

4. In order to explain the mechanism of the alkylating action of acid chlorides we studied the effect of temperature on diethylphosphoric acid anilide. It was shown that heating it to 230° formed dimethylaniline (85%). A preliminary scheme for decomposition of diethylphosphoric acid anilide has been presented.

LITERATURE CITED

[1] B. A. Arbuzov and B. P. Lugovkin, J. Gen. Chem. 21, 1869 (1951). *

[2] Ch. Gibson, D. Vining, J. Chem. Soc. 123, 831, Chem. Zentr. 1923, III, 33.

[3] Toy, J. Am. Chem. Soc. 66, 499 (1944); Rueggerberg and Chernack, J. Am. Chem. Soc. 70, 1802 (1948).

[4] Noller and Dutton, J. Am. Chem. Soc. 55, 425 (1933).

* See Consultants Bureau English translation p. 2075.

[5] Billman, Radike, Mundy, J. Am. Chem. Soc, 64, 2977 (1942).

[6] A. R. Todd, J. Baddiley, V. M. Clark, J. J. Michalski, J. Chem. Soc. 1949, 815.

[7] A. E. Arbuzov and B. P. Lugovkin, J. Gen. Chem. 6, 401 (1936).

[8] McCombie, Saunders, Stacey, J. Chem. Soc., 1945, 381.

[9] loc.cit. page 382.

[10] G. Steinberg, J. Org. Chem. 15, 644 (1950).

[11] G. Steinberg, J. Org. Chem. 15, 644 (1944); Gerrard, J. Chem. Soc. 1940, 218.

[12] A. Skita, F. Keil, H. Havemann, Ber., 66, 1408 (1933).

[13] Beilstein, Handbuch. A. Org. Chem. XII, 62, 160, 164 (1929); Erstes Ergbd., XII, 155, 158, 159 (1933); S. Komatsu, Chem. Zentr., I, 800 (1913).

[14] Beilstein, XII, 1265, 1274, 1275 (1929); 534 (1933).

[15] A. E. Chichibabin, R. A. Konovalova, and A. A. Konovalova, J. Russ. Phys. Chem. Soc. 53, 193 (1921); F. Bergstom, H. Sturz, H. Tracy, J. Org. Chem. 11, 245 (1946); N. F. Turitsina and A. F. Vompe, Proc. Acad. Sci. USSR 64, 509 (1950).

[16] J. Braun, Ber., 36, 3525 (1903); 37, 2814 (1904).

A. M. Butlerov Chemical Institute
V. I. Ulyanov-Lenin Kazan State University
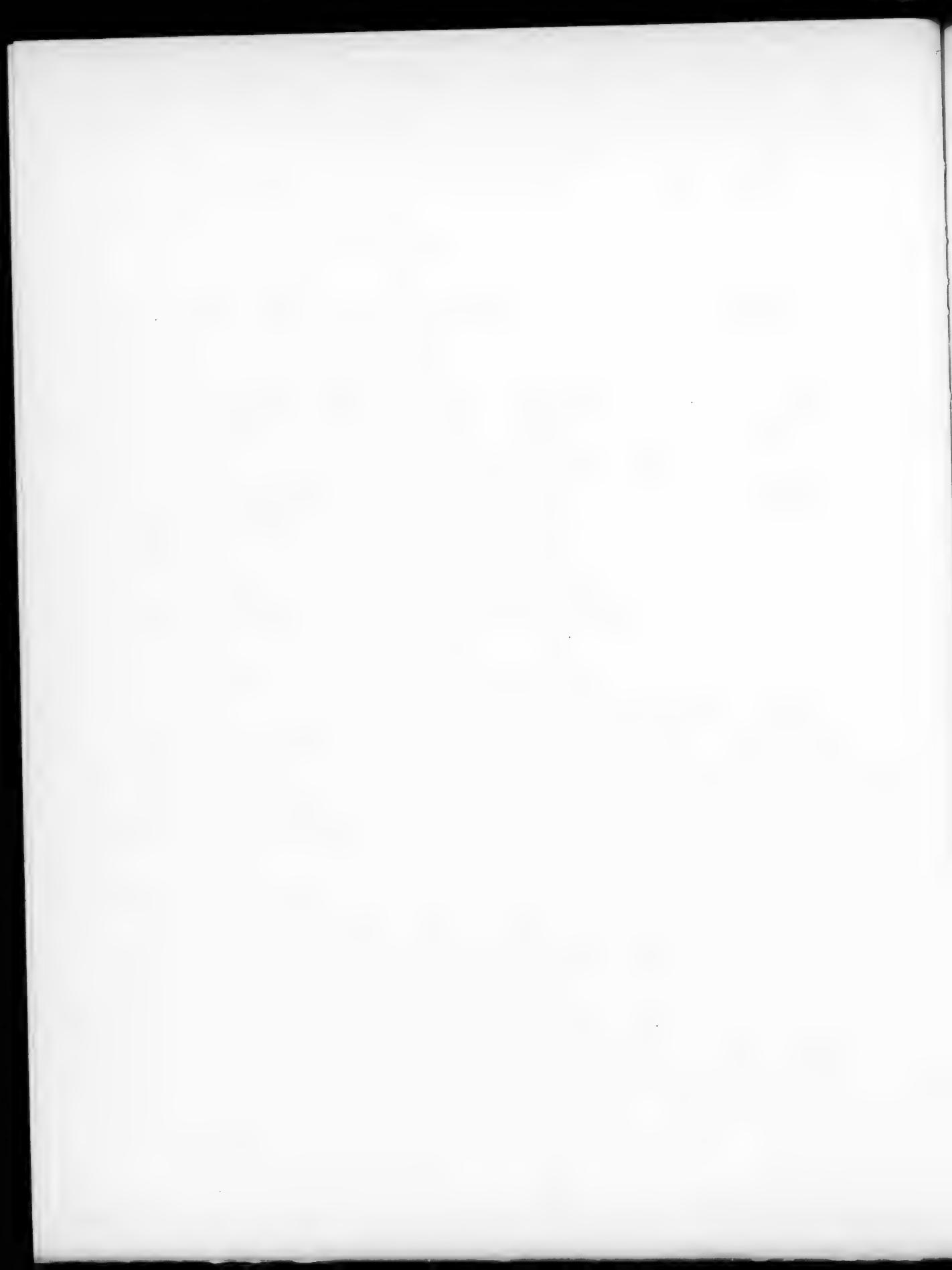
VIII. ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO ETHYLIDENE- AND BENZYLIDENE-MALONIC AND ACETOACETIC ESTERS

A. N. Pudovik

In a series of earlier papers [1] we showed that dialkylphosphorous acids add very readily to a,β-unsaturated ketones, aldehydes, nitriles, esters of unsaturated acids, and esters of vinyl alcohols with formation of the corresponding saturated phosphonic ester derivatives. The preparation of many derivatives of phosphonic esters by this new method of synthesis is simple to perform, is practicable with regard to initial materials, and gives almost quantitative yields in most cases. In the course of our earlier work on addition of dialkylphosphorous acids to esters of a,β-unsaturated acids which contained one activating group of the electronophilic type, we became interested in investigating the addition reaction of dialkylphosphorous acids to asymmetric unsaturated compounds containing two identical or different groups of the electronophilic type on a single carbon atom. It may be supposed that addition of dialkylphosphorous acids to compounds of this type would, on account of the simultaneous action of both activating groups on the double bond, proceed no less, and possibly even more, intensively than it did to the compounds studied earlier having one activating group. For this purpose in this present research we undertook to investigate the addition reaction of dialkylphosphorous acids to ethylidene-malonic ester, isopropylideneacetoacetic ester, benzylidene-malonic ester, and benzylideneacetoacetic ester. The reaction was carried out in the presence of catalysts — alkali metal alcoholates.

In order to avoid exchange of radicals in the process of reaction between the dialkylphosphorous acid being added and the alkali metal alcoholate, the latter was prepared from an alcohol containing the same radical as was present in the dialkylphosphorous acid.

Addition of dimethylphosphorous, diethylphosphorous, diisobutylphosphorous, and dibutylphosphorous acids to ethylidenemalonic ester was accompanied by vigorous heating of the reaction mixture, sufficient in some cases to cause boiling. Addition of the same dialkylphosphorous acids to ethylideneacetoacetic ester took place considerably more gently, accompanied by comparatively little heating of the reaction mix.

The yields of the addition products, which were the several ethyl esters of a-(dialkylphosphono)-ethylmalonic and a-(dialkylphosphono)-ethylacetoacetic acids, ranged from 65 to 87%. The formulas, constants, yields, and analytical results for phosphorous content of the products obtained are given in Table 1.

The product from addition of diethylphosphorous acid to ethylidenemalonic ester — the ethyl ester of a-(diethylphosphono)-ethylmalonic acid — was saponified by addition of hydrochloric acid with heating; as a product we obtained β-phosphonobutyric acid with m.p. 140-141°.

$$CH_3\!-\!CH\!-\!CH(COOC_2H_5)_2 \xrightarrow{+H_2O} CH_3\!-\!CH\!-\!CH\!-\!(COOH)_2 \xrightarrow{-CO_2} CH_3\!-\!CH\!-\!CH_2\!-\!COOH$$
$$(C_2H_5O)_2P=O \qquad\qquad (HO)_2P=O \qquad\qquad (HO)_2P=O$$
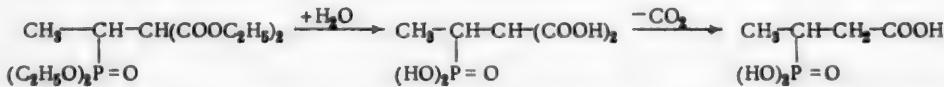
The β-phosphonobutyric acid prepared earlier by us, by saponification of β-diethylphosphonobutyric acid ethyl ester, had a melting point of 141-143°. The results which were obtained showed that addition of dialkylphosphorous acids to the double bond of ethylidenemalonic and ethylideneacetoacetic esters takes place in such a way that the dialkylphosphonic group adds to the β-carbon atom of the double bond, not carrying an activating group.

The full course of reaction for addition of dialkylphosphorous acids to ethylidenemalonic ester may be shown by the following scheme:

$$(RO)_2POH + RONa \longrightarrow (RO)_2P\!\!\begin{array}{c}O\\ \diagdown\\ Na\end{array} + ROH.$$

$$CH_3-CH=C(COOC_2H_5)_2 + \underset{O}{Na}P(OR)_2 \longrightarrow CH_3-CH-CNa(COOC_2H_5)_2 \text{ or}$$

$$CH_3-CH-C\overset{\displaystyle ONa}{\underset{\displaystyle COOC_2H_5}{\overset{\displaystyle |}{\underset{\displaystyle |}{}}}} \quad \xrightarrow{(RO)_2POH} \quad CH_3-CH-CH(COOC_2H_5)_2 + (RO)_2P\overset{O}{\underset{Na}{}}$$
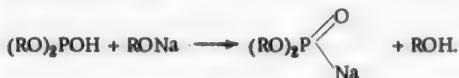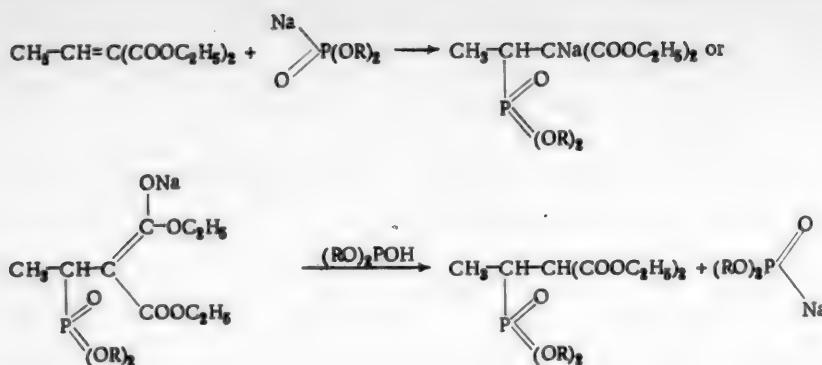
TABLE 1
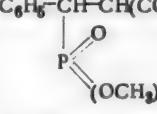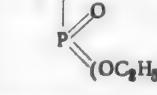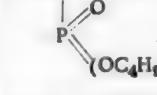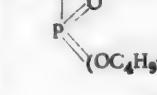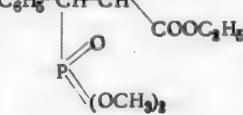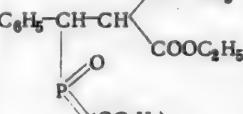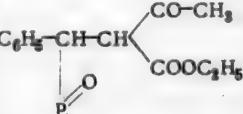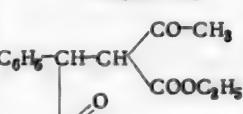
No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Phosphorous Content, (in %)		Yield (in %)
					found	calculated	
1	CH₃–CH–CH(COOC₂H₅)₂ |–P=O–(OCH₃)₂	181° (13 mm)	1.4462	1.1748	10.3	10.5	85.7
2	CH₃–CH–CH(COOC₂H₅)₂ |–P=O–(OC₂H₅)₂	180 (11 mm)	1.4427	1.1172	10.1	9.7	87.0
3	CH₃–CH–CH(COOC₂H₅)₂ |–P=O–(OC₄H₉-iso)₂	198–200 (11 mm)	1.4445	1.0445	8.1, 8.3	8.2	66.5
4	CH₃–CH–CH(COOC₂H₅)₂ |–P=O–(OC₄H₉-n)₂	203–204 (11 mm)	1.4457	1.0560	8.2, 8.2	8.2	78.0
5	CH₃–CH–CH(CO–CH₃)(COOC₂H₅) |–O–P–(OCH₃)₂	164–167 (14 mm)	1.4703	1.1943	11.7	11.7	71.1
6	CH₃–CH–CH(CO–CH₃)(COOC₂H₅) |–O–P–(OC₂H₅)₂	164–166 (12 mm)	1.4672	1.1473	10.6	10.6	65.6

In addition we investigated addition of dialkylphosphorous acids to benzylidenemalonic ester and to benzylideneacetoacetic ester. The reaction was performed in the same manner as was employed for the corresponding ethylidene derivative. This reaction also took place quite vigorously: with the lower dialkylphosphorous acids we observed boiling of the reaction mixture. The constants, yields, and analytical results for phosphorous content of all the ethyl esters of phenyldialkylphosphonomethylmalonic and phenyldialkylphosphonomethylacetoacetic acids are given in Table 2.

We may propose a scheme for the full course of the addition reactions of dialkylphosphorous acids to

ethylideneacetoacetic ester and to benzylidene- malonic and acetoacetic esters analogous to that given above for addition to ethylidenemalonic ester.

TABLE 2

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Phosphorous Content, (in %)		Yield (in %)
					found	calculated	
1	$C_6H_5-CH-CH(COOC_2H_5)_2$, P with O and $(OCH_3)_2$	200-202° (3 mm)	1.4975	1.2063	9.4	9.2	79.4
2	$C_6H_5-CH-CH(COOC_2H_5)_2$, P with O and $(OC_2H_5)_2$	212-214 (11 mm)	1.4911	1.1364	7.9, 7.9	8.0	70.0
3	$C_6H_5-CH-CH(COOC_2H_5)_2$, P with O and $(OC_4H_9\text{-iso})_2$	219 (14 mm)	1.4812	1.0475	6.8	7.0	80.9
4	$C_6H_5-CH-CH(COOC_2H_5)_2$, P with O and $(OC_4H_9\text{-n})_2$	218-220 (11 mm)	1.4820	–	7.2	7.0	75.6
5	$C_6H_5-CH-CH$ with $CO-CH_3$ and $COOC_2H_5$; P with O and $(OCH_3)_2$	193-195 (6 mm)	1.5295	1.2096	9.2, 9.4	9.2	65.4
6	$C_6H_5-CH-CH$ with $CO-CH_3$ and $COOC_2H_5$; P with O and $(OC_2H_5)_2$	204-206 (7 mm)	1.5195	1.1836	8.9	8.7	56.0
7	$C_6H_5-CH-CH$ with $CO-CH_3$ and $COOC_2H_5$; P with O and $(OC_4H_9\text{-iso})_2$	204-205 (6 mm)	1.4970	1.1104	7.8	7.5	66.6
8	$C_6H_5-CH-CH$ with $CO-CH_3$ and $COOC_2H_5$; P with O and $(OC_4H_9\text{-n})_2$	195-197 (1.5 mm)	1.4808	1.0441	7.7	7.5	67.8

In conclusion we performed experiments on addition of dialkylphosphorous acids to isopropylidenemalonic and isopropylideneacetoacetic esters. It was found, that even in these cases, despite the possible shielding effect of the two methyl groups attached to the β-carbon atom with the consequent reduction of its electronophilic nature as compared with the β-carbon atom in ethylidene- and benzylidene- derivatives, the addition reaction took place sufficiently vigorously with significant heating of the reaction mixture. However, it was not possible

to separate the addition products either by direct distillation of the reaction mixture or by working up in acetic acid and water; on heating a gradual increase in viscosity of reaction mass occurred, and it became converted progressively into a glassy almost solid product.

EXPERIMENTAL

General method for performing the addition reaction. The reaction of addition of dialkylphosphorous acids to ethylidenemalonic, ethylideneacetoacetic, benzylidenemalonic, benzylideneacetoacetic, isopropylidene- malonic, and isopropylideneacetoacetic esters was performed by the following general method. To 8-10 g ester was added an equimolar quantity of dialkylphosphorous acid and a saturated alcoholic solution of sodium alcoho- late was then added slowly to the mixture. The sodium alcoholate was prepared using an alcohol having the same radical as was present in the dialkylphosphorous acid being added. This latter condition appears most essential in performing the reaction under discussion; in the event that dialkylphosphorous acid be added to some idene derivative in presence of a sodium alcoholate containing a different radical, in consequence of exchange of radicals between the alcoholate and the dialkylphosphorous acid which takes place during the time of reaction [3], a mixture of addition products of both dialkylphosphorous acids to the idene derivative can form; separation of the mixture by distillation does not appear possible because of the close boiling points. In this latter circumstance separation of the addition products is possible only with a spread in boiling points and generally with increased phosphorous content compared with the theoretical value (particularly with use of sodium methylate for all of the reactions). Addition of the alcoholic alcoholate solution, particularly with lower dialkylphosphorous acids, was accompanied by vigorous heating of the reaction mixture, which in some cases (most frequently when the alcoholate was added rapidly) was sufficient to cause boiling. The addition of the alcoholate was continued in all cases until further addition to the reaction mixture did not cause heat release. In performing the reaction with the higher dialkylphosphorous acids we ordinarily used considerably larger quantities of the alcoholate than with the lower dialkylphosphorous acids. After addition of the necessary quantity of alcoholate solution, which varied in our experiments from several drops to several milliliters, the reaction mixture was heated for a short time on a water bath and then vacuum distilled. The addition products were colorless or lightly straw colored viscous liquids; several of them were quite readily soluble in water. Constants, yields, and the results of phosphorous analyses for all the prepared products are given in Tables 1 and 2.

Saponification of α-(diethylphosphono)-ethylmalonic acid ethyl ester. 3 g α-(diethylphosphono)-ethyl- malonic acid ethyl ester and 25 ml diluted (1:1) hydrochloric acid were heated in a sealed tube at 130-140° for a period of 10 hours. After opening the tube and removing the ethyl chloride, the solution was repeatedly evaporated, with periodic addition of distilled water —until hydrogen chloride was completely eliminated. The solution was then boiled a short while with animal charcoal, filtered, and evaporated on a water bath. After cooling and prolonged standing in the air, a precipitate of β-phosphonobutyric acid separated as a white powder. It was recrystallized twice from water to yield β-phosphonobutyric acid with m.p. 140-141°.

Phosphorous analysis, by Neyman method. Found %: P 18.2. $C_4H_9O_5P$. Calculated %: P 18.5.

SUMMARY

It has been shown that dialkylphosphorous acids in presence of alkali metal alcoholates add extremely readily to ethylidene- and benzylidene- malonic and acetoacetic esters to form, with yields of 65-80%, the corresponding ethyl esters of α-(dialkylphosphono)-ethylmalonic, and α-(dialkylphosphono)-ethylacetoacetic, phenyldialkylphosphono-methylmalonic, and phenyldialkylphosphono-methylacetoacetic acids.

LITERATURE CITED

[1] A. N. Pudovik, Proc. Acad. Sci. USSR,75, 499 (1950); A. N. Pudovik and B. A. Arbuzov, Proc. Acad. Sci. USSR, 75, 327 (1950); A. N. Pudovik, J. Gen. Chem., 22, 462, 467, 473, 1143, 1371 (1952). •

[2] A. N. Pudovik, J. Gen. Chem. 22, 1143 (1952). ••

[3] A. N. Pudovik and Yu. P. Kitaev, J. Gen. Chem. 22, 467 (1952). •••

• See Consultants Bureau English translation p. 525, 531,537, 1189, 1415.

•• See Consultants Bureau English translation p. 1189.

••• See Consultants Bureau English translation p. 531.

THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

IX. REACTION OF SODIUM DIETHYLPHOSPHITE WITH ALLYL BROMIDE AND WITH ISOMERIC CHLOROBUTENES

A. N. Pudovik and M. M. Frolova

In one of the contributions, relating to a study of the allyl rearrangement [1], we described a reaction between salts of dialkylphosphorous acid and the isomeric methoxychloropentenes; it was shown then that the reaction, depending on conditions, leads to formation of products which contain one or two dialkylphosphono groups. Using indirect methods, we established the conclusion that in this latter case addition of a molecule of dialkylphosphorous acid to the double bond takes place with formation of methoxydiethylphosphonopentene as the first stage of the reaction. Furthermore, in a special series of papers [2], one of us has shown that addition of dialkylphosphorous acid to unsaturated electronophilic reagents was a general reaction using: unsaturated nitriles, ketones, aldehydes, carboxylic acid esters, and esters of vinyl alcohols. We regard this reaction as the foundation for the development of a new, very simple and convenient, method for the synthesis of esters of various phosphonic acid derivatives.

In 1950 Rueggerberg, Chernack, and Rose [3], who were evidently unfamiliar with our work on the action of dialkylphosphorous acid salts on the isomeric methoxychloropentenes [1], described the reaction between sodium dibutylphosphite and allyl bromide and claimed to have prepared a high-boiling product, which they supposed, in accordance with the analytical data, to be either 1,2- or 1,3-di-(dibutylphosphono)-propane. They were not able to prepare the dibutyl ester of allylphosphonic acid, the synthesis of which appears to have been their aim. Regarding this reaction of allyl halides with salts of dialkylphosphorous acids as of considerable theoretical interest, both in relation to explaining the mechanism of the addition reaction as well as of the allyl rearrangement, we resumed our much earlier study and in the present work decided to study in greater detail the reactions between allyl bromide and the isomeric chlorobutenes with sodium diethylphosphite.

By performing the reaction between allyl bromide and sodium diethylphosphite in the minimum amount of benzene needed to dissolve sodium diethylphosphite, we obtained two high-boiling products. The first of these, which was formed with a 30.8% yield had a b.p. of 160-162° (3 mm), n_D^{20} 1.4430, d_4^{20} 1.1114; the other was prepared with a 11.2% yield and had a b.p. of 185-186° (3 mm), n_D^{20} 1.4500, d_4^{20} 1.1227. The phosphorous content of both products satisfied the same empirical formula $C_{11}H_{26}O_6P_2$. In accordance with studies made by us earlier it may be presumed that formation of these isomeric compounds results from addition of diethylphosphorous acid to the ethyl ester of allylphosphonic acid, i.e. they correspond to 1,2- and 1,3-di-(diethyl phosphono)-propanes. Actually the higher-boiling isomer, according to its constants, corresponds to 1,3-di-(diethylphosphono)-propane prepared by A. E. Arbuzov and Kushkova [4] and, considerably later, by Ford-Moore [5]. Synthesis of 1,3-di-(diethylphosphono)-propane in both of these cases was accomplished by the method of Academician Arbuzov involving action of trimethylene bromide on the fully ethylated ester of phosphorous acid. According to Ford-Moore, 1,3-di-(diethylphosphono)-propane has a b.p. of 175° (0.8 mm), $n_D^{16.5}$ 1.4508; according to the data of A. E. Arbuzov and Kushkova it boils at 186° at 3 mm and has d_0^{20} 1.12502.

Formation of 1,3-di-(diethylphosphono)-propane in our reaction may be shown by the following scheme:
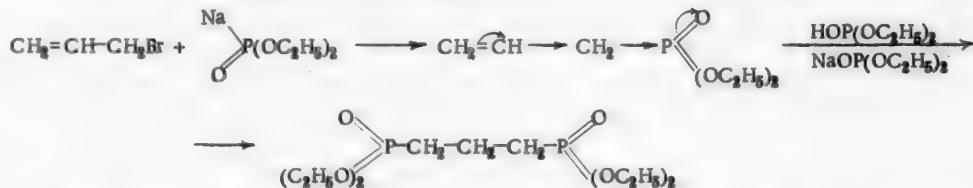
With regard to the main reaction product formed (with a b.p. of 160-162° at 3 mm), it evidently was 1,2-di-(diethylphosphono)-propane because it is not possible to form other isomeric products in the reaction

under study. It may be supposed that 1,2-di-(diethylphosphono)-propane is formed analogously to 1,3-di-(diethyl-phosphono)-propane by addition of diethylphosphorous acid to allylphosphonic ester, but in a different order. Naturally, such an assumption is improbable if one takes the polarization character of both reactants into account. It appears considerably more probable, in our opinion, to assume that allylphosphonic ester, which has a mobile three-carbon prototropic system, in the presence of alkoxyl ions which are active proton acceptors first isomerizes into the thermodynamically more stable propenylphosphonic ester, which then, like other α, β-unsaturated electronophilic reagents, readily adds to its double bond a molecule of diethylphosphorous acid.
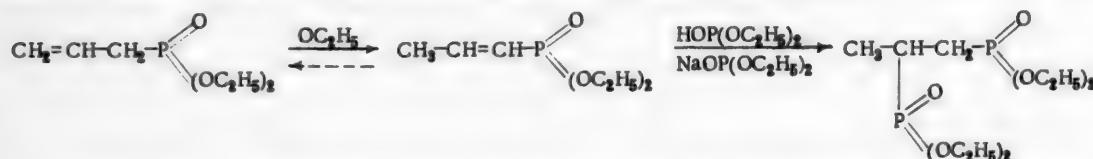
Actually, a series of authors, in particular Kohn and Linstid and their colleagues, have shown [6] that in the system $CH_2=CH-CH_2X \rightleftharpoons CH_3-CH=CH-X$, where X is an activating group of electronophilic character, the equilibrium is completely displaced toward the α, β-unsaturated form; this latter also appears applicable in the case of the system $CH_3-CH=CH-CH_2X \rightleftharpoons CH_3CH_2-CH=CH-X$.

Furthermore, we decided to study the effect of reaction conditions on the nature of the course of reaction, and in relation to the reaction products. When the reaction between sodium diethylphosphite acid and allyl bromide was performed with a considerable quantity of free diethylphosphorous acid present in the reaction mixture, (compared with data of the earlier work [1]), it was found that the ethyl ester of allylphosphonic acid was formed as the sole reaction product. Analogous results were obtained, even when an excess of diethylphosphorous acid was not present in the reaction mixture, in the presence of a large quantity of benzene. With comparatively small quantities of benzene in the reaction mixture we obtained all three products: both isomeric di-(diethylphosphono)-propanes as well as the ethyl ester of allylphosphonic acid. Thus, the interesting fact developed that the course of the reaction between allyl bromide and sodium diethylphosphite effectively changes in nature depending on the quantity of diethylphosphorous acid or inert diluent present in the reaction medium. In the presence of large quantities of the latter the reaction stops at the substitution stage, with a minimum content — the addition reaction proceeds almost quantitatively.

As a development of the last conclusion and in order to fully explain the mechanism of formation of di-dialkylphosphono derivatives in the reaction between allyl halide compounds with salts of dialkylphosphorous acid, we conducted experiments on the direct addition of diethylphosphorous acid to the ethyl ester of allylphosphonic acid. It was found that in the presence of sodium ethylate at 90-100° the reaction goes very slowly, at 130-140° it takes place considerably more rapidly; as a result of heating for three hours we obtained 1,3-di(diethylphosphono)-propane, b.p. 159-160° (2 mm), n_D^{20} 1.4420, d_4^{20} 1.1117, with 51.6% yield. Isomeric products were not observed. The results of the latter experiment may be regarded as direct evidence of the correctness of the mechanism proposed by us for formation of di-diethylphosphono derivatives in the reaction described above.

In addition, we studied the reaction of sodium diethylphosphite with the isomeric chlorobutenes. As a result of the action of sodium diethylphosphite on an equimolar quantity of 1-chlorobutene-2 in an ether solution we obtained 1-diethylphosphonobutene-2 with a 45.2% yield. The reaction took place very readily and quickly. In performing the analogous reaction with the second chloride — 2-chlorobutene-3 — we found that it took place only very slowly in ether solution; because of this, subsequent tests were performed in a benzene solution. By reaction of sodium diethylphosphite on 2-chlorobutene-3 in the presence either of diethylphosphorous acid or of a large quantity of benzene, we observed the formation of only one product — 1-diethylphosphonobutene-2. Addition of bromine to 1-diethylphosphonobutene-2 gave 1-diethylphosphono-2,3-dibromobutane. The structure of 1-diethylphosphonobutene-2 was established by oxidizing it with potassium permanganate; acetic acid was identified among the oxidation products.

Thus the reaction between 2-chlorobutene-3 and sodium diethylphosphite takes place with a complete allyl rearrangement and may be shown by the scheme:
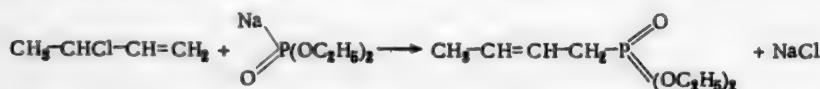
In performing the reaction between sodium diethylphosphite and 2-chlorobutene-3 with free diethylphosphorous acid and excess benzene absent from the reaction medium, instead of 1-diethylphosphonobutene-2 we obtained the high boiling product 1,2-di-(diethylphosphono)-butane in a 15% yield, b.p. 160-161° (3 mm), n_D^{20} 1.4420, d_4^{20} 1.1014. This same product was obtained in 59.3% yield by direct addition of diethylphosphorous acid to 1-diethylphosphonobutene-2 in the presence of sodium ethylate. For both the first and the second cases, the reaction may be expressed by the following scheme:
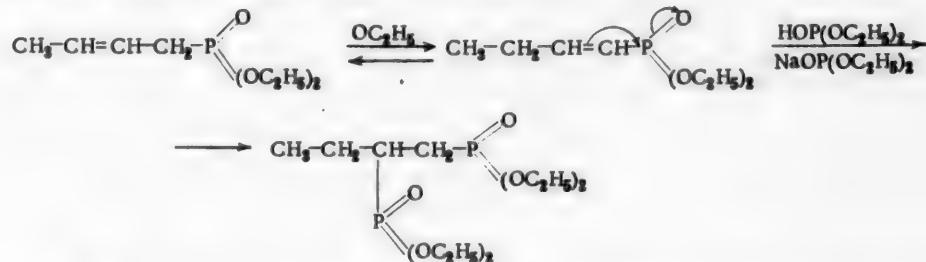
Thus, the effect of the inert diluent, in the 3-chlorobutene-2 experiments, on the course of the reaction with salts of dialkylphosphorous acid is completely determined, and the mechanism proposed for formation of di-dialkylphosphono derivatives confirmed.

EXPERIMENTAL

Reaction of sodium diethylphosphite on allyl bromide. Test I. 7.6 g sodium and 50 ml absolute benzene were placed in a round bottom flask fitted with a reflux condenser and dropping funnel; 46 g diethylphosphorous acid was then slowly added. After all the sodium dissolved, with formation of a solution of sodium diethylphosphite, 40 g allyl bromide was gradually added. The reaction took place very violently with considerable heating of the reaction mix. After the entire quantity of allyl bromide had been added, the reaction mixture was heated on a water bath for 3 hours, and later after cooling, treated with a small quantity of water. After separating the upper layer and drying it for a short while over calcium chloride, the benzene was distilled from it; the residue was vacuum distilled. Two products were separated:

1) 1,2-Di-(diethylphosphono)-propane (8 g), b.p. 160-162° (3 mm); n_D^{20} 1.4430; d_4^{20} 1.1114; MR_D 75.18. Calculated 74.74. Found %: P 19.47. $C_{11}H_{26}O_6P_2$. Calculated %: P 19.62.

2) 1,3-Di-(diethylphosphono)-propane (3 g), b.p. 185-186° (3 mm); n_D^{20} 1.4500; d_4^{20} 1.1227; MR_D 75.38. Calculated 74.74. Found %: P 19.71. $C_{11}H_{26}O_6P_2$. Calculated %: P 19.62.

Test II. The reaction was carried out with the same quantities of reactants but with a somewhat larger quantity of benzene. As a result of distillation of the reaction mixture we separated 12.2 g 1,2-di-(diethylphosphono)-propane having a b.p. of 160-162° (3 mm); 7.8 g 1,3-di-(diethylphosphono)-propane with b.p. 185-187° (3 mm); and 11 g diethyl ester of allylphosphonic acid with b.p. 98-100° (12 mm).

Reaction of sodium diethylphosphite on allyl bromide in the presence of excess diethylphosphorous acid. The benzene solution of sodium diethylphosphite was prepared analogously to the foregoing from 3.8 g sodium 45.6 g diethylphosphorous acid, and 30 ml benzene. 20 g allyl bromide was then added to it. After the end of the reaction, the reaction mixture was treated with water, the benzene layer dried with calcium chloride, and then after distillation of the benzene on a water bath the residue was vacuum distilled. We separated 22.7 g diethylphosphorous acid and 7.7 g 1-diethylphosphonopropene-2 with a b.p. of 98-100° (12 mm), n_D^{20} 1.4350, d_4^{20} 1.0370, MR_D 44.80. $C_7H_{15}O_3P$. Calculated 44.93. Found %: P 17.15. $C_7H_{15}O_3P$. Calculated %: P 17.40.

Reaction of sodium diethylphosphite on allyl bromide in the presence of a large quantity of benzene. The benzene solution of sodium diethylphosphite was prepared from 3.8 g sodium, 22.8 g diethylphosphorous acid, and 150 ml benzene. 20 g allyl bromide were taken for the reaction. As a result of performing the reaction we obtained 5.7 g diethylphosphorous acid and 16.3 g allylphosphonic acid ethyl ester with a b.p. of 99-100° (12 mm), n_D^{20} 1.4348, d_4^{20} 1.0368.

Addition of bromine to allylphosphonic acid ethyl ester. To 5.5 g allylphosphonic acid ethyl ester, dissolved in 10 ml carbon tetrachloride, was added, while cooling and with agitation, a solution of 2.5 g bromine in 20 ml carbon tetrachloride. After addition of the entire quantity of bromine, the reaction mixture turned

yellow. By distillation of the reaction mixture we separated 2 g of a fraction with b.p. 76-148° (4 mm) and 3.2 g 1,2-dibromo-3-diethylphosphonopropane with a b.p. of 148° (4 mm), n_D^{20} 1.4880, d_4^{20} 1.5730. Found %: P 9.37. $C_7H_{15}O_3PBr_2$. Calculated %: P 9.17.

Addition of diethylphosphorous acid to the ethyl ester of allylphosphonic acid. 6 g allylphosphonic acid ethyl ester and 7 g diethylphosphorous acid were heated in a sealed tube, in the presence of sodium ethylate, at 130-140° for a period of 4 hours. By distillation of the reaction mixture we separated 5.4 g of a substance with a b.p. of 159-160° (2 mm), n_D^{20} 1.4420; d_4^{20} 1.1117.

Preparation of the isomeric chlorobutenes. 3 heavy-walled bottles containing about 400 ml concentrated hydrochloric acid, were cooled in a freezing mixture (−15°) and about 100 g distilled bivinyl added. The bottles were tightly sealed with rubber stoppers and placed on a shaker. Agitation was continued at room temperature for a total period of about 30 hours. The bottles were then opened and the upper layers, containing the chloride, were separated from all of the bottles and combined, washed with a dilute soda solution and with water, then dried over calcium chloride, and distilled through a meter column filled with small glass rings. After several distillations we obtained 62 g 1-chloro-2-butene with a b.p. of 84-85°, n_D^{20} 1.4350 and 80.6 g 3-chloro-1-butene with a b.p. of 64-65°, n_D^{20} 1.4150.

Reaction between sodium diethylphosphite and 1-chloro-2-butene. An ether solution of sodium diethylphosphite was prepared from 6.3 g sodium, 37.8 g diethylphosphorous acid, and 300 ml dry ether. We then added, slowly and with agitation, 25 g 1-chloro-2-butene, after which the reaction mixture was heated on a water bath for 3 hours. At the end of the reaction, sodium chloride was filtered off and washed with ether; the ether in the ether solution was distilled on a water bath after brief drying over calcium chloride, and the residue was distilled under vacuum. We obtained about 5 g of unreacted diethylphosphorous acid and 24 g diethylphosphonobutene-2 with a b.p. of 121.5-122° (19 mm), n_D^{20} 1.4380, d_4^{20} 1.0219, MR_D 49.32. $C_8H_{17}O_3P$. Calculated 49.54. Found %: P 15.84. $C_8H_{17}O_3P$. Calculated %: P 16.14.

Reaction of sodium diethylphosphite on 3-chloro-1-butene. Experiment 1. A benzene solution of sodium diethylphosphite was prepared from 7.4 g sodium, 44.4 g diethylphosphorous acid, and 50 ml benzene. Unreacted small fragments of sodium were mechanically removed from the solution using a long thin needle. We added 30 g 3-chloro-1-butene slowly with stirring to the benzene solution of sodium diethylphosphite which had thus been made completely transparent, after which the reaction mixture was heated for 3 hours on a water bath. Precipitated sodium chloride was then filtered, the benzene evaporated from the filtrate on a water bath, and the residue distilled under vacuum. We obtained 12.8 g diethylphosphorous acid, 18 g 1-diethylphosphonobutene-2 with a b.p. 96-98° (6 mm), n_D^{20} 1.4380 and 6.8 g 1,2-di-(diethylphosphono)-butane with a b.p. of 160.-161° (3 mm), n_D^{20} 1.4420, d_4^{20} 1.1014, MR_D 79.28. Calculated 79.35. Found %: P 19.06. $C_{12}H_{28}O_6P_2$. Calculated %: P 18.78.

Saponification of 1,2-di-(diethylphosphono)-butane with dilute hydrochloric acid at 130-140° gave a thick, pale-yellow colored oil which did not crystallize on standing.

Experiment II. (in the presence of excess diethylphosphorous acid). To a benzene solution of sodium diethylphosphite prepared from 3.7 g sodium, 44.4 g diethylphosphorous acid, and 50 ml benzene, was added 15 g 3-chloro-1-butene. The reaction mixture was heated on a water bath for 3 hours. Sodium chloride was then removed by filtration, the benzene evaporated on a water bath, and the residue distilled under vacuum. Even at the very start of distillation, signs of decomposition of the product were noted; because of this the distillation was stopped and the product worked up in water and benzene. As a result of the last distillation we obtained 18 g diethylphosphorous acid, 8.7 g 1-diethylphosphonobutene-2 having a b.p. of 113-114° (14 mm), n_D^{20} 1.4380, d_4^{20} 1.0221 and 3.6 g of lower-boiling fractions.

Experiment III. (in the presence of a large quantity of benzene). To a benzene solution of sodium diethylphosphite, prepared from 3.7 g sodium, 22.2 g diethylphosphorous acid, and 150 ml benzene, we added 15 g 3-chlorobutene-1. As a result of carrying out the reaction and working up the reaction product, we obtained 7.2 g diethylphosphorous acid, 9.5 g 1-diethylphosphonobutene-2, and about 3 g lower-boiling fractions. Repetition of the experiment with larger quantities of reagents gave analogous results. In this experiment, as in the previous one, 1,2-di-(diethylphosphono)-butane was not observed.

Addition of diethylphosphorous acid to 1-diethylphosphonobutene-2. 7 g diethylphosphorous acid and 5 g 1-diethylphosphonobutene-2 with a small quantity of sodium ethylate were heated in a sealed tube at 130-140° for 3 hours. By distilling the reaction mixture, we obtained 4.8 g 1,2-di-(diethylphosphono)-butane with a b.p. of 159-161° (3 mm), n_D^{20} 1.4420, d_4^{20} 1.1016.

Addition of bromine to 1-diethylphosphonobutene-2. To 6 g 1-diethylphosphonobutene-2 we slowly added, with cooling and stirring, a solution of 2.6 g bromine in 20 ml carbon tetrachloride. The liquid was rapidly decolorized during the reaction; at the end of the addition it developed a stable yellow color. After standing for 24 hours it was vacuum distilled. We obtained 6.7 g 1-diethylphosphono-2,3-dibromobutane with a b.p. of 148-150° (3 mm), n_D^{20} 1.4890, d_4^{20} 1.5427, MR_D 65.86. Calculated 65.54. Found %: P 8.45. $C_8H_{17}O_3PBr_2$. Calculated %: P 8.80.

Oxidation of 1-diethylphosphonobutene-2 by potassium permanganate. 12 g 1-diethylphosphonobutene-2 was dissolved in 400 ml water; 26.4 g finely powdered potassium permanganate was then slowly added to the solution with continuous stirring. The temperature of the reaction mixture was held below 10° by cooling the flask in running water. The manganese dioxide was then filtered off, taken up in boiling water and filtered again. Both filtrates were combined and concentrated to a volume of 30-50 ml, treated with hydrochloric acid and steam-distilled. The distillate was neutralized with ammonia and silver acetate was then precipitated from it.

Analysis of the silver salt: 0.5228 g substance: 0.3360 g Ag. Found %: Ag 64.28. $C_2H_3O_2Ag$. Calculated %: Ag 64.61.

SUMMARY

1. The reaction of sodium diethylphosphite with allyl bromide and with isomeric chlorobutenes was studied.

2. It was shown that the presence in the reaction medium of excess diethylphosphorous acid or benzene plays an effective role in the course of these reactions. In their presence the reaction stops at the substitution stage with the formation of allylphosphonic ester and 1-dialkylphosphonobutene-2; in the absence of free diethylphosphorous acid from the reaction medium and in the presence of only the minimum quantity of benzene needed to dissolve the sodium diethylphosphite, sodium diethylphosphite added to the double bond of the allylphosphonic ester with formation of di-dialkylphosphono derivatives.

3. It was shown that the reaction between sodium diethylphosphite and 3-chloro-butene-2 takes place with a complete allyl rearrangement.

4. The addition of diethylphosphorous acid, in the presence of sodium ethylate, to allylphosphinic ester and to 1-diethylphosphonobutene-2 was shown by direct experiments.

LITERATURE CITED

[1] A. N. Pudovik, Thesis presented at session of Acad. Sci. USSR, Div. Chem. Sci., Kazan (1947); A. N. Pudovik and B. A. Arbuzov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 522 (1949).

[2] A. N. Pudovik, Proc. Acad. Sci. USSR, 75, 499 (1950); A. N. Pudovik and B. A. Arbuzov, Proc. Acad. Sci. USSR, 75, 327 (1950); A. N. Pudovik, J. Gen. Chem., 22, 462, 467, 473, 1143, 1371 (1952). •

[3] W. Rueggerberg, J. Chernack and J. Rose, J. Am. Chem. Soc. 72, 5336 (1950).

[4] A. E. Arbuzov and N. P. Kushkova, J. Gen. Chem. 6, 284 (1936).

[5] A. Ford-Moore, and J. Williams, J. Chem. Soc. 1465 (1947).

[6]see D. Beker. Tautomerism. Moscow. (1937).

• See Consultants Bureau English translation page 525, 531, 537, 1189, 1415.

TRIPHENYLBIPHENYLPHOSPHONIUM SALTS

G. V. Medoks and V. F. Andronova

Triphenylaryl- and triphenylalkylphosphonium salts have acquired considerable practical significance in recent times because of application of some of them in analytical chemistry [1] and in the separation of elements which are very similar in properties. These materials are also useful as insecticides [2]. They are also used for protection of woolen materials and furs from damage by moths [3]. There are indications of the possible use of compounds of this type in medicine, and also as plasticizers and as dye-fixing substances. Although several triphenylarylphosphonium salts have been described in the literature, for example the tetraphenylphosphonium [4] and triphenyl-α-naphthylphosphonium [5] salts, nevertheless many other similar compounds, among them the triphenyl-4-biphenylphosphonium salts, had not been prepared up to the present time. In order to prepare quartenary phosphonium salts, in which the phosphorous atom is directly bonded to carbon atoms of the aromatic ring, we may use either the reaction of oxygen on an ether solution of triphenylphosphine together with an organo-magnesium compound, as proposed by Ya. Ya. Dodonov and G. V. Medoks [4], or the reaction of triphenylphosphine with halide substituted aromatic hydrocarbons which takes place with the assistance of catalyst — anhydrous aluminum chloride [6].

We found that cuprous chloride, used as catalyst for analogous reactions, assured a satisfactory reaction course and did not require, in contrast to aluminum chloride, protection from moisture or careful purification in order to avoid side reactions.

We prepared triphenyl-4-biphenylphosphonium bromide, using the above catalyst, from triphenylphosphine and 4-bromo-diphenyl in an 18.3% yield based on triphenylphosphine. A compound of triphenylphosphine and cuprous chloride — $(C_6H_5)_3P \cdot CuCl$ — was also separated from the reaction products. We prepared a solution of the free base, and using this formed triphenyl-4-biphenylphosphonium nitrate, chloride, and sulfate. The formation of a series of other salts is also described. A solution of triphenyl-4-biphenylphosphonium hydroxide did not decompose on boiling, but in the presence of a small quantity of sodium hydroxide boiling led to decomposition of the base according to the equation:

$$[(C_6H_5)_3(C_6H_5C_6H_4)P]OH \longrightarrow (C_6H_5)_3PO + C_6H_5C_6H_5.$$

A similar catalytic activity of alkali has been reported earlier by G. V. Medoks [5].

EXPERIMENTAL

Triphenyl-4-diphenylphosphonium bromide. A mixture, containing 2.6 g triphenylphosphine prepared by the Pfeifer method as modified by Dodonov and Medoks [4], 2.3 g 4-bromo-diphenyl with a m.p. of 89° synthesized according to the procedures of Schmidt and Schultz [7], and 0.5 g cuprous chloride, was heated in a round-bottomed flask on a paraffin bath for 2 hours at 240° and 1 hour at 280°. The reaction product solidified on cooling and was a yellowish glassy mass. It was worked up in ethyl alcohol, and the solution filtered by suction from the separated crystalline precipitate (1.58 g).

The alcoholic solution was evaporated to dryness on a water bath and the residue extracted several times with hot water. The water extracts were combined, filtered, and boiled down. The crystals (0.90 g) with a m.p. of 231° which separated on cooling were recrystallized from water.

0.5894 g substance: 0.1339 g H_2O. Found %: H_2O 22.71. $C_{30}H_{24}BrP \cdot 8H_2O$. Calculated %: H_2O 22.55.

Water of crystallization was completely lost at 110-120°.

0.0423 g and 0.0407 g substance: 8.85 ml and 8.52 ml $AgNO_3$ (T= 0.00163). Found %: Br 16.04 and 16.05. $C_{30}H_{24}BrP$. Calculated %: Br 16.14.

Triphenyl-4-biphenylphosphonium bromide was a colorless substance, readily soluble in water, ethyl alcohol, and chloroform, but insoluble in benzene, benzine, and ethyl ether.

Cuprous chloride addition product with triphenylphosphine. The residue insoluble in alcohol (1.58 g) referred to above was dissolved in chloroform and precipitated by ethyl ether. Colorless crystals, containing chloroform of crystallization. For quantitative iodometric determination of copper, a portion of the substance, free of chloroform of crystallization, was first decomposed with nitric acid (specific gravity 1.4), but for determination of chlorine, by the Moore method, the material was first dissolved in pure chloroform and then decomposed using concentrated ammonia with subsequent heating until excess ammonia was removed.

0.2500 g substance: 17.00 ml $Na_2S_2O_3$ (T = 0.00642). 0.0600 g substance: 17.30 ml $AgNO_3$ (T = 0.00163). Found %: Cu 17.55; Cl 9.81. $C_{18}H_{15}ClPCu$. Calculated %: Cu 17.60; Cl 9.82.

A chloroform solution of this material when treated with a strong solution of ammonia deposits, on vaporization of the solvent, colorless crystals with a m.p. of 79° which were shown to be triphenylphosphine (mixture test). Thus the material which was insoluble in alcohol was an addition product of cuprous chloride and triphenylphosphine.

A small quantity of this substance (1 g) along with 1 g of the initial 4-bromodiphenyl was separated by fractional crystallization of the material (2.85 g) which was insoluble in water on extraction (see above) of triphenyl-4-biphenylphosphonium bromide.

Triphenyl-4-biphenylphosphonium hydroxide and salts. By reaction of an aqueous solution of triphenyl-4-biphenylphosphonium bromide with a suspension of freshly precipitated silver hydroxide in water, a solution of the free base was formed which showed a strong alkaline reaction. This solution was neutralized with the respective acid to yield, after the solution was boiled down and crystallized, the chloride, sulfate, or nitrate; these were colorless crystalline materials, readily soluble in water, ethyl alcohol, and chloroform but insoluble in benzene, benzine, and ethyl ether. The salts were dried in a vacuum dessicator.

0.1032 g substance: 23.69 ml $AgNO_3$ (T = 0.00163). Found %: Cl 7.81. $C_{30}H_{24}ClP$. Calculated %: Cl 7.87. 0.2896 g substance: 0.0699 g $BaSO_4$. Found %: S 3.32. $C_{60}H_{48}P_2SO_4$. Calculated %: S 3.46.

Triphenyl-4-biphenylphosphonium salts dissolved in water reacted with solutions of iodides, thiocyanates, chromates, bichromates, and permanganates to form precipitates which were difficultly soluble in cold water and appreciably soluble in boiling water.

SUMMARY

1. A new catalyst has been proposed for the reaction of triphenylphosphine with halide-substituted aromatics which has several advantages as compared with anhydrous aluminum chloride.

2. Triphenyl-4-biphenylphosphonium salts and a solution of the free base were prepared.

LITERATURE CITED

[1] G. V. Medoks and A. V. Krylov, J. Appl. Chem. 13, 1529 (1940); G. V. Medoks and N. Markelova, J. Anal. Chem. 1, 319 (1946); G. V. Medoks and L. V. Eferova, Sci. Rep., Saratov State University (1952).

[2] Guy, Chem. Zentr, 1938, I, 158.

[3] English patents 303092, 3261371; Dutch Patent 95565; German Patent 506987.

[4] Ya. Ya. Dodonov and G. V. Medoks, Ber., 61, 907 (1928).

[5] G. V. Medoks, J. Appl. Chem. 8, 298 (1938).

[6] J. Chatt and F. Mann, J. Chem. Soc. 1940, 1193.

[7] Schmidt and Schultz, Ann., 174, 207 (1874).

SYNTHESIS OF ALIPHATIC ORGANO-ELEMENTAL COMPOUNDS BY THE DIAZO METHOD

V. SYNTHESIS OF COMPOUNDS OF ELEMENTS OF THE IV GROUP – ORGANO-LEAD COMPOUNDS

A. Ya. Yakubovich, E. N. Merkulova, S. P. Makarov, and G. I. Gavrilov

Utilization of the extreme reactivity of aliphatic diazo derivatives for preparation of elemento-organo compounds has been limited, until recent times, only to the synthesis of organo-mercury compounds [1]. We were able to show that organic derivatives of P, As, Sb, Bi, Si, and Sn could be prepared by the same method [2].

In this present paper we give the results of our study on the reaction of diazomethane and diazoethane on lead halides. It should be noted that until now only a few organo-lead compounds were known containing a substituted aliphatic radical [3].

Attempts to alkylenate lead chloride by diazomethane were not successful. In tests in ethereal media as well as in other solvents and both in the presence and in the absence of catalysts, although the diazomethane was decomposed no formation of organo-lead compounds was observed. This latter may be explained, naturally, by the fact that lead chloride is practically insoluble in the organic solvents usually used for preparation of solutions of aliphatic diazo compounds. Evidently under these conditions interaction of the reagents is difficult.

It was practically impossible to use a solution of lead tetrachloride because even at temperatures of -15-$20°$, this material, on the one hand, chlorinated the solvent, and on the other hand, rather rapidly decomposed spontaneously (for example in a CCl_4 medium) with release of chlorine and lead chloride. Alkylenation was also not successful using a stable salt of chloroplumbic acid – $(NH_4)_2PbCl_6$, a derivative of lead tetrachloride, because the solubility of this salt in organic solvents is no greater than that of lead chloride.

Lead tetraacetate, which is readily soluble in benzene, easily reacts with diazomethane, with liberation of nitrogen; naturally organo-lead compounds are not formed in this manner, and the reaction follows the scheme:

$$Pb(OCOCH_3)_4 + CH_2N_2 \longrightarrow CH_2(OCOCH_3)_2 + Pb(OCOCH_3)_2 + N_2.$$

Only with triethylchloro lead and diethyldichloro lead, which are relatively readily soluble in ether, was it possible to observe, on reacting them with diazomethane, formation of the corresponding chloromethyl derivative. However, the alkylenation reaction takes place in this case only in unusual conditions, somewhat different from the conditions employed in other cases. On mixing an ether solution of diazomethane with alkyl lead chloride no reaction was observed either cold or on heating. If copper bronze were added to the mixture, then (at temperatures of 10-15°) gradual decomposition of diazomethane started, during which the precipitate of undissolved lead chloride diminished and the reaction led to formation of chloromethyl lead compounds:

$$CH_2N_2 \xrightarrow{Cu} [CH_2] \xrightarrow{ClPB(C_2H_5)_3} (C_2H_5)_3PbCH_2Cl$$

$$(C_2H_5)_2PbCl_2 \xrightarrow{CH_2} [(C_2H_5)_2PbCl(CH_2Cl)] \xrightarrow{CH_2} (C_2H_5)_2Pb(CH_2Cl)_2.$$
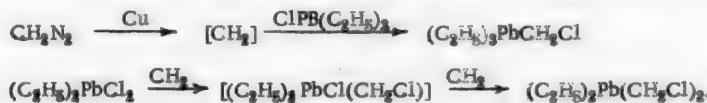
In the reaction described of diazomethane with ethyl lead chloride, in addition to the chloromethyl lead derivative we usually observed formation of a small amount of tetraethyl lead. It is most probable that formation of this takes place as a result of a secondary process of reduction of the initial ethyl lead halide compound by methylene to a lead-alkyl radical, which then disproportionates to form tetraethyl lead. However, formation of tetraethyl lead is also possible as a result of a reaction, which is analogous to one given below for diazoethane. Formation of tetraethyl lead together with the chloromethyl derivative makes purification of the latter considerably more difficult. However, by repeated vacuum distillation it was possible to obtain chloromethyltriethyl and di-(chloromethyl)-diethyl lead in a comparatively pure state. Di-(chloromethyl)-diethyl lead, in contrast to chloro-methyltriethyl lead, was a poorly stable compound which decomposed with separation of a precipitate even on storage in the dark.

Diazoethane, like diazomethane, would not react with triethyl lead chloride in absence of catalysts, and

the reaction, observed only in presence of copper bronze, led to formation of unstable triethyl-α-chloroethyl lead, which we were not able to separate from the reaction mixture. On removal of solvent (ether) even at temperatures of minus 15° (under vacuum), the product which remained decomposed into lead chloride and tetraethyl lead.

EXPERIMENTAL

1. Preparation of diethyl-di-(chloromethyl)-lead. A mixture of 24 g dichlorodiethyl lead with a small amount of copper bronze (0.1-0.2 g) in 300 ml absolute ether was cooled to 0°. At this temperature and with good stirring we added one half of an ether solution of diazomethane, prepared by taking 2 moles diazomethane per mole of dichlorodiethyl lead plus a 10% excess. The temperature was then raised to 10-15°. During this we observed the release of bubbles of gas, the quantity of dichlorodiethyl lead decreased, and the solution gradually lost its initial yellow color. The solution was then again cooled to 0° and the second portion of diazomethane added.

When the solution was barely yellow and gas evolution ceased, stirring was discontinued, and the reaction mixture allowed to stand overnight. The residue (4.3 g) was then filtered off and the filtrate distilled. After the ether was removed a liquid containing a small amount of precipitate and brown tar remained which was vacuum distilled with a dephlegmator. At 2 mm at a temperature of 86-98° 9.6 g of material came over. After repeated vacuum distillation we separated a colorless mobile liquid with a peculiar odor having a b.p. of 96° at 2 mm; d_4^{20} 1.9890. The material was soluble in absolutely dry organic solvents and insoluble in water.

3.995 mg substance: 3.065 mg AgCl. 0.8380 g substance: 0.6984 g $PbSO_4$. Found %: Pb 56.93; Cl 18.98. $C_6H_{14}PbCl_2$. Calculated %: Pb 56.86; Cl 19.5.

2. Preparation of chloromethyl-triethyl lead. A mixture containing 25 g triethylchloro lead in 260 ml absolute ether together with 0.1-0.2 g copper bronze, was treated with diazomethane (as in experiment I) although the chlorotriethyl lead went into solution completely. Diazomethane was taken on the basis of 1 mole diazomethane (with a 10% excess) per mole of chlorotriethyl lead. Under vacuum distillation at 10 mm and at temperatures of 83-99° a colorless mobile liquid distillate (21.7 g) was obtained. The product thus prepared was a mixture of chloromethyltriethyl lead and tetraethyl lead. Based on its halide content, the mixture contained 73% chloromethyltriethyl lead.

After two or three vacuum distillations with a dephlegmator we were able to separate comparatively pure chloromethyl-triethyl lead with a b.p. of 65.5-66.5° at 3 mm; d_4^{20} 1.7917; n_D^{20} 1.5434. The substance was a mobile liquid with a peculiar odor.

4.313 mg substance: 1.609 mg AgCl. 0.4032 g, 0.3064 g substance: 0.3548 g, 0.2708 g $PbSO_4$. Found %: Pb 60.36, 60.1; Cl 9.23 $C_7H_{17}PbCl$. Calculated %: Pb 60.25; Cl 10.33.

3. Reaction of diazoethane on triethylchloro lead. To a mixture of 10 g triethylchloro lead, 120 ml absolute ether, and 0.15 g copper bronze we added during a period of one hour at 0° (with stirring) a dry solution of 5.2 g diazoethane in 170 ml ether. The temperature was brought up to ambient and a precipitate (3 g) which appeared to be $PbCl_2$ removed from the light green solution by filtration. The ether was distilled under vacuum, during this the remaining oil again separated $PbCl_2$ to the extent of 1 g. Vacuum distillation of the residue gave 5 g of a heavy colorless liquid, whose properties were identical with tetraethyl lead: b.p. 74-75° at 4 mm; n_D^{20} 1.5139; d_{16}^{20} 1.655.

4. Reaction of diazomethane with lead tetraacetate. To a solution of 5 g dry lead tetraacetate in 100 ml absolute benzene we added during a period of one hour at 2° a dry solution of 3.5 g diazomethane in 150 ml benzene while cooling the mixture in ice water. The mixture was allowed to stand at room temperature overnight. It was filtered from the residue, which contained lead diacetate, and the benzene distilled off with a dephlegmator; the residue was vacuum distilled twice. During this we separated methylene diacetate (2 g) with a b.p. of 61° at 3 mm (b.p. according to Butlerov [4] is 170° at 760 mm).

4.620 mg substance: 7.688 mg CO_2; 2.803 mg H_2O. 5.200 mg substance: 8.710 mg CO_2; 2.975 mg H_2O. Found %: C 45.38 C 45.68; H 6.79, 6.40. $C_5H_8O_4$. Calculated %: C 45.45; H 6.04.

SUMMARY

The reactions of diazomethane with lead chloride, with a salt of chloroplumbic acid, with lead tetra-acetate, with diethyldichloro lead and with triethylchloro lead were studied.

It was found that reaction of organo-lead chlorides with diazomethane takes place only in the presence of

copper bronze catalyst, which promotes the decomposition of the aliphatic diazo compound and leads to formation of the corresponding chloromethyl lead derivative.

Diazoethane reacts with triethylchloro lead in the presence of copper bronze to form unstable triethyl-α-chloroethyl lead, which decomposes into tetraethyl lead and lead chloride.

Lead chloride and ammonium chloroplumbate do not form organo-lead compounds with diazomethane under these conditions.

Lead tetraacetate readily reacts with diazomethane to form methylene diacetate and lead diacetate.

LITERATURE CITED

[1] A. Nesmeyanov, G. Povkh, Ber., 67, 971 (1934); L. Hellerman, M. Newman, J. Am. Chem. Soc. 54, 2859 (1933).

[2] A. Yakubovich, S. Makarov, J. Gen. Chem., 22, 1528 (1952);*G. Braz, A. Yakubovich, J. Gen. Chem., 11, 41 (1941); A. Yakubovich, V. Ginsburg, J. Gen. Chem., 22, 1534 (1952). **

[3] A. Nesmeyanov, R. Freidlina, K. Kocheshkov, Bull. Acad. Sci. U.S.S.R., 1948, 127; K. Kocheshkov, Bull. Acad. Sci. U.S.S.R., 1948, 127; K. Kocheshkov, A. Aleksandrov, Ber., 67, 527 (1934); P. Austin, J. Am. Chem. Soc., 53, 3514 (1931).

[4] A. Butlerov, Ann, 107, 111 (1858).

Received February 21, 1951
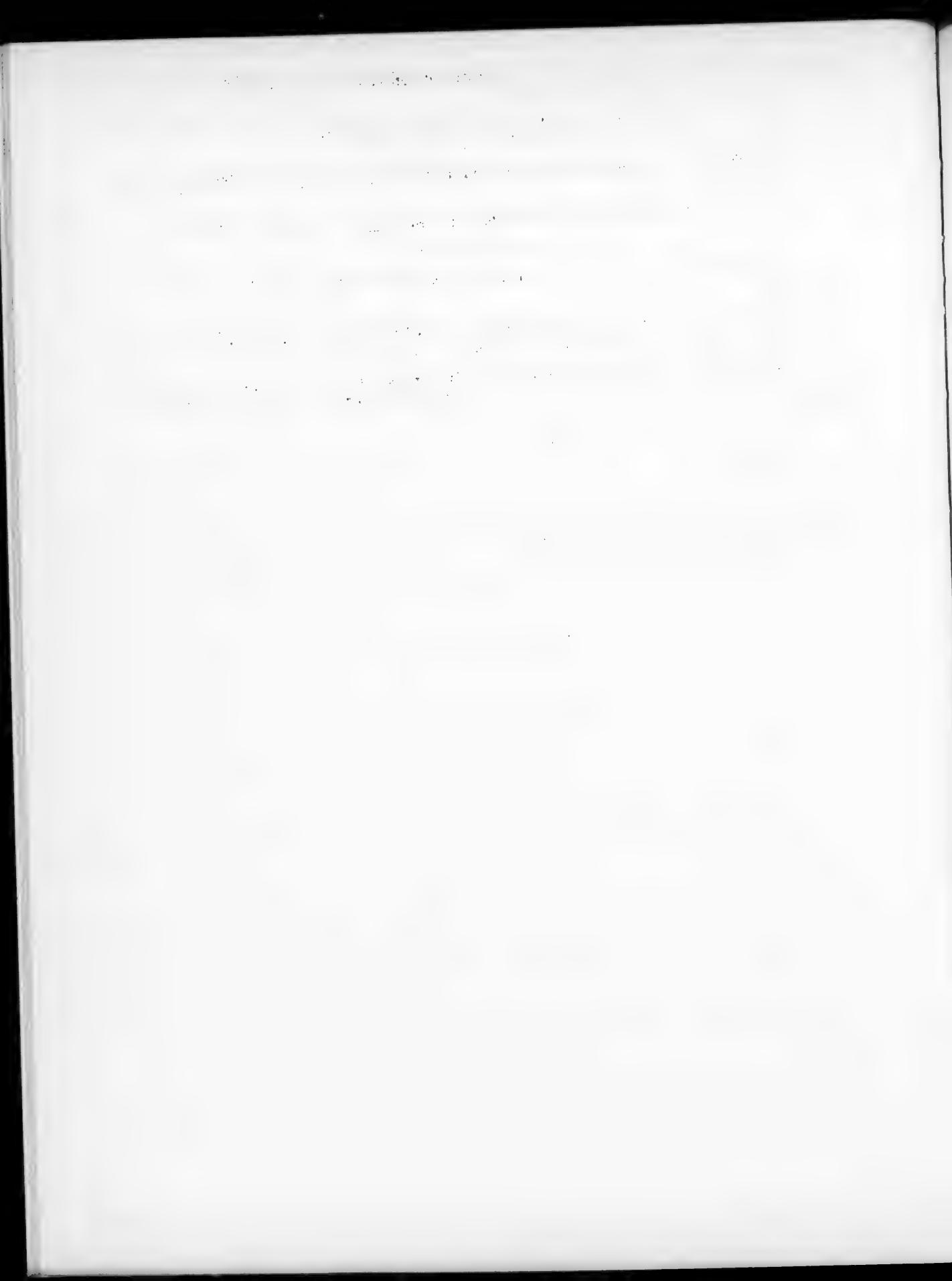
PHOTOREACTIONS OF ORGANOMETALLIC COMPOUNDS OF MERCURY IN SOLUTION

XI. THE REACTIONS OF β-DINAPHTHYLMERCURY

Yu. A. Oldekop

In one of our earlier papers [1] we studied the behavior of the α-naphtyl-radical, formed by photoreactions of α-dinaphthylmercury in several organic media. It was noted that the α-naphthyl-radical, formed by photolysis of α-naphthylmercury in carbon tetrachloride, did not remove chloride from the latter to form α-chloronaphthalene, but led to redistribution of hydrogen among the naphthyl radicals. It was known to us from the literature [2] that α- and β-dinaphthoylperoxides form, on thermal dissociation in a carbon tetrachloride medium, the corresponding α- and β-chloronaphthalenes. With this in mind it appeared of interest to extend our studies of photoreactions to β-dinaphthylmercury.

We found that photoreaction of β-dinaphthylmercury in carbon tetrachloride gave naphthalene and a small amount of uncrystallizable tarry material, just as in the similar reaction of α-dinaphthylmercury. Thus the photoreaction of β-dinaphthylmercury in carbon tetrachloride differs from thermal dissociation of β-dinaphthoylperoxide in the same solvent.

Among the other products of the photoreaction of β-dinaphthylmercury in carbon tetrachloride, we obtained calomel in a quantitative yield and hexachloroethane. By exposure of β-dinaphthylmercury in chloroform or 1,2-dichloroethane to ultra-violet light, a quantitative yield of calomel was obtained. The naphthyl-radical in this case takes hydrogen from the solvent and forms naphthalene. In the experiments with chloroform, in addition, hexachloroethane is found. The formation of calomel in chlorinated organic media on photoreaction of β-dinaphthylmercury in them, should be probably attributed to the subsequent photodissociation of β-naphthylmercury chloride.

From organic media which did not contain halides we selected ethyl cellosolve; the photoreaction of β-dinaphthylmercury took place very slowly in it with the formation of metallic mercury and naphthalene.

The very low solubility of β-dinaphthylmercury in organic compounds markedly reduced the velocity of its photodissociation in comparison with α-dinaphthylmercury. No difference was observed in the behaviour of the β-naphthyl radical formed in comparison with α-naphthyl radicals

EXPERIMENTAL

β-Dinaphthylmercury in carbon tetrachloride. 0.5 g β-dinaphthylmercury in 20 ml carbon tetrachloride were exposed for 120 hrs. At the end of the exposure the precipitate was filtered and dried. It was calomel (blackened by concentrated ammonia); it weighed exactly 0.25 g (quantitative yield). The filtrate was distilled on a water bath. The residue was steam distilled, a white substance with the odor of hexachloroethane and naphthalene solidified in the condenser. We were able, by partial sublimation of this material over concentrated sulfuric acid, to separate pure hexachloroethane with an m.p. of 185° (in a sealed capillary). The melting point of a material known to be hexachloroethane was not depressed by this substance. The remaining portion of the substance was shown to be naphthalene by the melting point of its picrate, m.p. 149° (according to the literature it should be 150°). The residue after steam distillation contained a small amount of tarry products.

β-Dinaphthylmercury in chloroform. 0.5 g β-dinaphthylmercury was exposed in 12 ml chloroform. The exposure lasted for 180 hours. The reaction mass gradually turned a dark brown color. At the end of the exposure, the precipitate was filtered (noticeable traces of mercury in it) and dried. It was shown to be calomel (blackening with concentrated ammonia), its weight was exactly 0.25 g (quantitative yield). Chloroform was evaporated from the filtrate on a water bath. After double distillation, we were able to extract from the distillate some hexachloroethane, m.p. 186° (after sublimation above concentrated sulfuric acid). This material did not depress the melting point of a known pure preparation of hexachloroethane. The residue from the first distillation was steam distilled. A white crystalline substance solidified in the condenser; this was shown to

be naphthalene, its weight was 0.1 g. The melting point of this material was 80° (from alcohol). The material did not depress the melting point of pure naphthalene.

β-Dinaphthylmercury and 1,2-dichloroethane. 0.5 g β-dinaphthylmercury in 10 ml 1,2-dichloroethane was exposed for 180 hours. After exposure traces of mercury were noted. The precipitate was filtered, it weighed exactly 0.25 g. It was calomel (blackening with concentrated ammonia). From the filtrate before steam distillation we extracted 0.1 g naphthalene, m.p. 79°. This material did not depress the melting point of known naphthalene.

β-Dinaphthylmercury and ethylcellosolve. 0.5 g β-dinaphthylmercury in 20 ml ethylcellosolve was exposed for 400 hours. At the end of the exposure the precipitate was filtered. 0.18 g metallic mercury was found in it (82% of theoretical), together with unreacted β-dinaphthylmercury; m.p. 237° (from dichloroethane), weight 0.08 g (16% of initial). The filtrate was diluted with water, a white floc separated which was filtered and recrystallized from alcohol; its weight was 0.15 g, m.p. 80°. This material did not depress the melting point of a pure sample of naphthalene.

All the experiments on exposure to ultra-violet light were performed in sealed long narrow quartz tubes with an internal diameter of 8 mm. A PRK-2 lamp was used as the light source.

SUMMARY

1. β-Dinaphthylmercury reacts with carbon tetrachloride when exposed to ultra-violet light with formation of calomel, naphthalene, hexachloroethane, and tarry materials.

2. Photoreaction of β-dinaphthylmercury in chloroform gives calomel, naphthalene, and hexachloroethane. In the analogous reaction of β-dinaphthylmercury in 1,2-dichloroethane, calomel and naphthalene form.

3. In photoreaction of β-dinaphthylmercury in ethylcellosolve, metallic mercury and naphthalene were formed.

LITERATURE CITED

[1] G. A. Razuvaev and Yu. A. Oldekop, J. Gen. Chem., 20, 506 (1950). •

[2] M. Kharasch and R. Donnley, J. Org. Chem. 10, 406 (1945).

REDUCTION OF PYRIDINE AND ITS HOMOLOGS ON THE
DROPPING MERCURY ELECTRODE

A. G. Pozdeeva and E. M. Gepshtein

We selected, as subjects for study, pyridine, β- and γ-picolines, and 2,6-lutidine. References exist in the literature [1-3] on the reduction of pyridine on the dropping mercury electrode; the homologs of pyridine to all appearances have not been studied by anyone up to the present time.

Preparation of products for study. Many methods are given in the literature, in the form of patents for the most part, for separation of the mentioned pyridine homologs from their corresponding fractions. However, it is difficult in practice to prepare pure β- and γ-picoline and 2,6-lutidine from their fractions because of the lack of specific procedures and methods for separation of these products.

In the present research, we utilized several suggestions for their preparation from the literature [4-7], but we defined the separate steps of the process more accurately, and recommend the scheme given here for separation of pyridine homologs from the β-picoline fraction.

Preparation of 2,6-Lutidine. To 238 g of a narrow boiling β-picoline fraction heated in a flask with a reflux condenser on a boiling water bath, was added a hot saturated solution of 200 g urea in 108 ml water. The reaction mixture was heated for a period of one hour on a boiling water bath with agitation. The solution was then slowly cooled over a 6 hour period. The crystals of 2,6-lutidine-urea which separated were suction filtered on a Buchner funnel. The filtrate was set aside for preparation of β- and γ-picolines. The crystals of the 2,6-lutidine-urea complex were airdried for a 10-15 hour period and then decomposed by water (we used 1 liter of water for 200 g of the complex). 2,6-Lutidine was in the

Figure 1. Cooling Curve for 2,6-lutidine.

water layer after decomposition of the complex, and was extracted from it by ether. The ether was then vaporized on the water bath, and the residue in the flask was raw 2,6-lutidine; it was thoroughly dried with anhydrous caustic. After two precipitations of 2,6-lutidine by urea, as described above, the product had a crystallization temperature of minus 23°. The 2,6-lutidine was subsequently fractionally crystallized 7 times, as a result of which we were able to raise the crystallization temperature of our sample of 2,6-lutidine to minus 8.4°. This product was thoroughly dried over caustic and distilled from a flask with a small nozzle. The one-degree fraction which was separated solidified at minus 6.5°. The purity of the prepared product was determined by a thermographic method, i.e., by the curve of freezing point temperatures versus time (Figure 1).

Preparation of γ-picoline. The fraction which was freed of 2,6-lutidine was treated with a solution of calcium chloride. To 356g of the fraction, heated to 60-70° on a water bath, we added in small portions with stirring a hot solution of 570 g crystalline calcium chloride dissolved in 36 ml water. After addition of the entire calcium chloride solution, the reaction mixture was stirred for 10 minutes and the solution then slowly cooled over a 5-6 hour period, after which the crystals of the complex compound of γ-picoline and calcium chloride which were obtained were filtered by suction on a Buchner funnel and dried on a watch glass in a slightly warm drying oven. The filtrate was reserved for preparation of β-picoline. The dry crystals of the complex were decomposed by water at room temperature, and the base extracted from the water solution using ether; the ether was then evaporated on a water bath leaving γ-picoline as a residue in the flask which was then precipitated a second time with calcium chloride.

After two precipitations of γ-picoline using a solution of calcium chloride, we obtained 87 g raw γ-picoline.
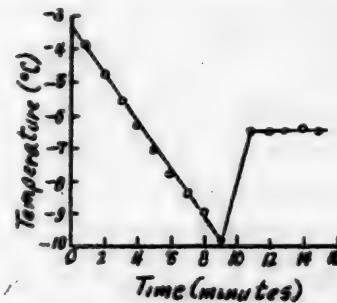
This product was distilled from a flask with a 48-hook dephlegmator (effectively 1-2 theoretical plates). The fraction boiling at 143.5° (50.5 g) was pure γ-picoline and solidified at 2.6° (Figure 2).

Preparation of β-picoline. The fraction which had been freed from 2,6-lutidine and γ-picoline was polymerized using elemental sulfur. To 108 g of the fraction which contained β-picoline with a small admixture of γ-picoline, was added 33 g sulfur and 1,1 g zinc chloride. The reaction mixture was heated in a flask fitted with a reflux condenser on a hot plate for 40 hours. An additional 20 g sulfur and 1 g zinc chloride were added to the cooled reaction mixture, and the mixture again heated to boiling for a period of 24 hours. The unreacted β-picoline was then removed by steam distillation. The distillate was salted out using solid caustic, the β-picoline was separated from the aqueous layer and thoroughly dried with anhydrous caustic. The product so prepared was distilled in a flask fitted with a 48-hook dephlegmator. The


Figure 2. Cooling Curve for γ-picoline

fraction boiling within the limits 142.4-142.6° (35 g) was β-picoline, which was then purified by two treatments with phthalic anhydride. Thus, to 26.5 g β-picoline we added 6.7 g acetic anhydride and 6.7 g phthalic anhydride.

The mixture was heated in a flask with a reflux condenser for 4 hours on a water bath. The contents of the flask were then poured into 100 ml water and the solution made strongly alkaline to litmus with 50% NaOH solution. The solution was then filtered, and a rather small quantity of dark brown colored precipitate was found on the filter— this was a condensation product of γ-picoline and

Figure 3. Cooling curve for β-picoline

2,6-lutidine with phthalic anhydride (pysophthalones). From the filtrate, which contained a solution of β-picoline, was distilled an azeotropic mixture of β-picoline and water at 97-98°. After the distillate was treated with solid caustic, the upper layer − β-picoline −was separated from water and dried with anhydrous caustic. After two purification treatments with phthalic anhydride, we obtained β-picoline which solidified at minus 19.4° (Figure 3).

Preparation of pyridine. Pyridine was obtained from the pyridine fraction by repeated fractionation in a column. The characteristics of the product obtained (as compared with literature data) may be seen in the table.

As may be seen from the tables the products prepared were pure pyridine, 2,6-lutidine, β- and γ-picoline. Slight differences in the freezing points, amounting to tenths of a degree, may be explained by the difficulty of determining the melting points of these products because they are all strongly hygroscopic materials.

EXPERIMENTAL

In order to prepare the polarograms, we used a visual polarograph manufactured by UFAN in 1947 (Sverdlovsk) and a galvanometer of the Leningrad Institute for Construction of Physics Equipment with a current sensitivity of 2.77×10^{-9} A mm/m. All measurements were made at a temperature of $25 \pm 0.1°$. A saturated calomel electrode was used as the anode and its potential was taken as zero. We used in this work a capillary with a dropping period of 2.4 seconds. For reduction studies on the pyridines, we took them as solutions in 50% ethyl alcohol. An 0.1 N solution of LiCl in 50% alcohol was used as an electrolyte. In order to remove atmospheric oxygen from the solution under test, we passed hydrogen through the solution for a 15-20 minute period. The half wave potential was determined by the wave equation (1):

$$E = E_{1/2} - \frac{0.0591}{n} \log \frac{i}{I-i}, \qquad (1)$$

where i is the current strength at voltage E, and I is the diffusion current.

Graphically, this equation gives a straight line with slope $0.0591/n$ when $\log \frac{i}{I-i}$ is plotted as a function of E. The point on the straight line where $\log \frac{i}{I-i} = 0$, i.e., where $\frac{i}{I-i} = 1$ and $i = \frac{1}{2}I$, corresponds to the half wave potential, as may be seen from the wave equation. We determined the value of the half wave potential in this manner.

Flowchart

β-Picoline fraction (base content 85 %)
↓
Purification of fraction via sulfate; distillation in a column
↓
Sharp β-picoline fraction, 142.2-143° (100% base content)
↓
Double treatment with urea and with phthalic acid

From "Double treatment with urea and with phthalic acid":
- → 2,6-Lutidine-urea complex → Decomposition of complex → "Raw" 2,6-lutidine → Seven-fold fractional crystallization → 2,6-Lutidine concentrate; solidifying temp. −8.4° → Distillation of 2,6-lutidine concentrate → 2,6-Lutidine; solidifying temp. −6.5°
- ↓ Fraction containing β-γ-picoline → Double treatment with CaCl₂ → γ-Picoline-CaCl₂ complex → Dissociation of complex → Raw γ-picoline → Distillation of raw γ-picoline → γ-Picoline; solidifying temp. 2.60°
- → Fraction containing β-picoline → Double polymerization with sulfur for 64 hours → Raw β-picoline → Distillation of the raw β-picoline → β-Picoline → Double purification by treatment with phthalic anhydride → β-Picoline, solidifying temp. −19.4°

Constant	Pyridine		2,6-Lutidine		γ-Picoline		β-Picoline		Literature ref.
	Our data	Literature values	Our data	Literature values	Our data	Literature values	Our data	Literature values	
Density	0.9780 (25°)	0.978(25°) 0.981	0.9241 (15°)	0.915(16°) 0.932(25°)	0.9572 (20°)	0.957 (20°)	0.9510 (20°)	0.952(20°)	[7-11]
Boiling point	115.3°	116° 115.2 115.3 115.4	144.4°	142.8° 144.2 144.4 144.7	144.9°	143.1° 144.6	144.0°	142-143° 143.8 143.9 144.0	
Index of Refraction	1.5010 (20°)	1.5091	1.5000 (16°)	1.4996 (16°)	1.5050 (20°)	1.5052 (20°)	0.5050 (20°)	1.5040 (20°) 1.5043 (24°)	
Melting point	−41°	−42°	−6.5°	−6° −6.3 −6.5	+2.6°	+3° +3.5 +3.8	−19.4°	−17.9° −18.3 −18.7	

Fig. 4

Potential (voltage with reference to saturated calomel electrode)
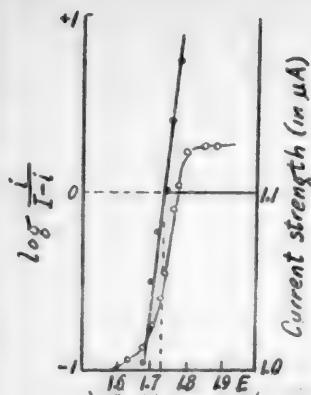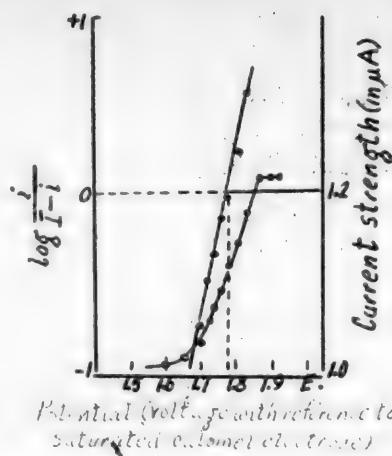
Fig. 5
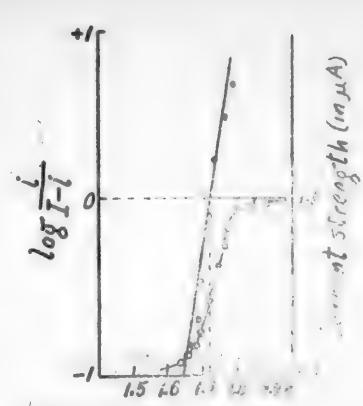

Fig. 6

Fig. 7

Reduction of pyridine, 2,6-lutidine, β- and γ-picoline. For polarography we used solutions of the pyridine bases in 50% ethyl alcohol, the concentration of which ranged from 5 to 10 m.moles per liter. Against a background which contained 0.1 N lithium chloride in 50% ethyl alcohol, pyridine, 2,6-lutidine, β- and γ-picoline were reduced on the dropping mercury electrode and gave satisfactory expression of diffusion current.

The experimental data obtained for pyridine and its homologs, both the relation of $\log\frac{i}{I-i}$ with E as well as the half wave potentials are given in figures 4-7.

As may be seen from the given data, pyridine, 2,6-lutidine, β- and γ-picoline are polarographically active materials, i.e., they are reduced by a dropping mercury electrode. γ-Picoline is the most difficult to reduce ($E_{1/2} = -1.83$V), β-picoline is the easiest ($E_{1/2} = -1.72$ V), 2,6-lutidine has a half wave potential of minus 1.78 V, and pyridine one of minus 1.73 V — all relative to the saturated calomel electrode.

SUMMARY

1. A study has been made of the reduction of pyridine and some of its homologs by the dropping mercury electrode.

2. The half wave potentials for pyridine, 2,6-lutidine, β- and γ-picoline have been determined.

3. A scheme for separation of 2,6-lutidine and β- and γ-picoline from an industrial 8 mixture is proposed

LITERATURE CITED

[1] I. M. Kolthoff and J. J. Lingane. Polarography. State Sci.-Tech. Press, 370 (1948) [2] nikova and I. A. Korshunov, J. Phys. Chem., 4, 503 (1948) [3] S. Wawzonek, Anal. Chem. 21, Riethof, Amer. Pat. 2,295,606; Chem. A., 1132 (1943). [5] G. Riethof, Amer. Pat. 2,376,608; (1943). [6] G. Riethof, S. Richards, S. Savitt, D. Othmer, Ind. Eng. Chem. An. Ed., 18, 458 (1946) acki, C. Winans, Amer. Pat 2,402,158; Chem. A. 6102 (1946). [8] Technical Encyclopedia, Chemical and Technological Data., 8, 47, 49 (1932). [9] Beilst., IV, 104, supplement IV, 81. [10] Chauman, Chemistry of coal utilization, 2, 1361 (1945). [11] I. L. Liplavk and E. P. Bolstei, J. Appl. 191 (1951). (See Consultants Bureau English translation page 207).

ELECTROLYTIC REDUCTION OF LEPIDINE

II. ELECTROLYTIC REDUCTION OF LEPIDINE IN AN ALKALINE MEDIUM

V. V. Levchenko and A. A. Zats

By chemical reduction of lepidine in an alkaline medium, Williams [1] obtained a yellowish oil, which on boiling with dilute nitric acid gave a red colored crystalline product. Williams regarded this product as the nitrate of lepidine $C_{20}H_{18}N_2 \cdot HNO_3$. There are no literature references on the electrolytic reduction of lepidine in alkaline media.

Our studies showed, that lepidine on electrolytic reduction in alkaline media gives the dimer of dihydrolepidine, which was prepared by us by electrolytic reduction of lepidine in acid media [2]; in addition we were able to establish the formation of dihydrolepidine monomer, which was stable for a long time in a mixture of lepidine and tetrahydrolepidine. Monomeric dihydrolepidine forms during further treatment of the electrolyte two additional oxidation products.

Electrolytic reduction of lepidine was performed in an alkaline alcohol-water solution using a cellophane diaphragm. We used a mercury cathode and a platinum anode. In a large number of experiments we investigated the effect of many factors on the process of electrolytic reduction of lepidine, namely: voltage, current density, temperature, length of electrolysis, and alkali concentration. The highest yield of reduction products was obtained on a renewed mercury cathode using a current density of 26.6 amperes per square decimeter, electrolysis for 45 minutes, temperature 16-19°, as was observed in studies by Levchenko [3,4].

By electrolytic reduction of lepidine in alkaline media, we obtained three crystalline products having m.p.'s of 279, 236, and 203°, and also liquid tetrahydrolepidine.

Properties of the product melting at 279°. According to its properties, the given product was proven to be completely identical to the dimer of dihydrolepidine, prepared by us by electrolytic reduction of lepidine in acid media. This was confirmed by ultimate analysis of the product and of its picrate, by determination of its molecular weight (Rast method), and also by determination of the melting point of samples mixed with dihydrolepidine dimer (which had been prepared by electrolytic reduction of lepidine in acid media) which was not depressed. Dihydrolepidine dimer was not formed if the electrolysis was performed at high temperatures.

The dimer of dihydrolepidine was converted into tetrahydrolepidine by chemical reduction by boiling for several hours in concentrated hydrochloric acid with tin.

Properties of the product melting at 236°. The material did not dissolve in alkali and was readily soluble in acids with formation of salts. Ether and ligroin were the organic solvents in which it was not soluble; it dissolved readily in chloroform when cold, and in alcohol, benzene, toluene, and xylene when heated. It did not give a color with a solution of potassium bichromate in sulfuric acid. It was not affected by electrolytic reduction in acid media; chemical reduction by boiling for 5 hours in concentrated hydrochloric acid and tin led to tetrahydrolepidine. Ultimate analysis and determination of the molecular weight gave its elemental content which corresponds to the formula $(C_{10}H_{10}N)_2O$.

This product formed a picrate melting at 242°. Ultimate analysis of the picrate confirmed the formula given above for dihydrolepidine oxide, prepared according to the equation:

$$2C_{10}H_{11}ON - H_2O = (C_{10}H_{10}N)_2O.$$

Properties of the product melting at 203°. The crystalline product with an m.p. of 203° which was obtained from the distillation flask after steam distillation of lepidine and tetrahydrolepidine sharply differed from the product with an m.p. of 236°; it was appreciably soluble in water, and was soluble not only in acids but also in alkalies. The aqueous solution was slightly fluorescent. It gave with potassium hydroxide a potassium salt which was readily hydrolyzed. The potassium salt was readily decomposed by carbonic acid. With

hydrochloric acid the product formed a hydrochloride, ... er reacted ... ... ium chlor... ... ... a double platinate having the composition of $[C_{10}H_{11}ON \cdot HCl]_2$ ... ... was ... ... determin... ion of the platinum content of this salt. It formed a derivative with ... ... whi ... ited at 233°; its nitrosoamine had an m p. of 235°, and it formed a methyl derivative (m ... ... le did not give a color with a solution of potassium bichromate in sulfuric acid. We did not electrol... ... ... this product further in alkaline medium; in acid medium it was reduced to tetrahydrolepidine with ... ... anging from ... to 33% depending on length of electrolysis. Ultimate analysis and determination of its molecular weight gave its elemental content, which corresponded to the formula of hydroxydihydrolepidine: $C_{10}H_{11}ON$.

Hydroxydihydrolepidine formed a picrate, m.p 223-224°, the elemental analysis of which confirmed the formula given above for hydroxydihydrolepidine.

Hydroxydihydrolepidine $C_{10}H_{11}ON$ displays both basic and acid properties, and the structural formula of γ-hydroxydihydrolepidine may be tentatively ascribed to it, because a-hydroxydihydrolepidine which was prepared by Knorr and Klotz [5] by chemical reduction of a-hydroxylepidine has properties which differ from the product prepared by us.

Consequently, when the ether extract of the products from electrolytic reduction of lepidine in alkaline medium was stored in an open vessel in the air, polymerization of dihydrolepidine into the dimer occurred as well as formation of two more dihydrolepidine oxidation products. This indicates the presence, in the ethereal extract, of dihydrolepidine monomer, which is readily oxidized by atmospheric oxygen. This material is stable with time only in alkaline media; this is apparent because we were not able to obtain its oxidation products from the products of reduction of lepidine in acid media, despite our many attempts.

By action of more severe oxidizing agents (su... ... ... peroxide) on the ether extract from alkaline electrolysis, it was not possible to obtain hydroxydihy... ... ... these conditions oxidation goes farther and leads to formation of tarry materials. It wa... ... ... not possible ... separate the polymeric dihydrolepidine from the tetrahydrolepidine and residual unreacted lepidine, which accompanied ... despite many attempts to achieve this by distillation of the mixture under vacuum, fractional crystallization of their hydrochlorides prepared by treatment with hydrogen chloride, and other. The direction of the processes, as established by us, which take place during reduction of lepidine, may be presented in the form of the following scheme:
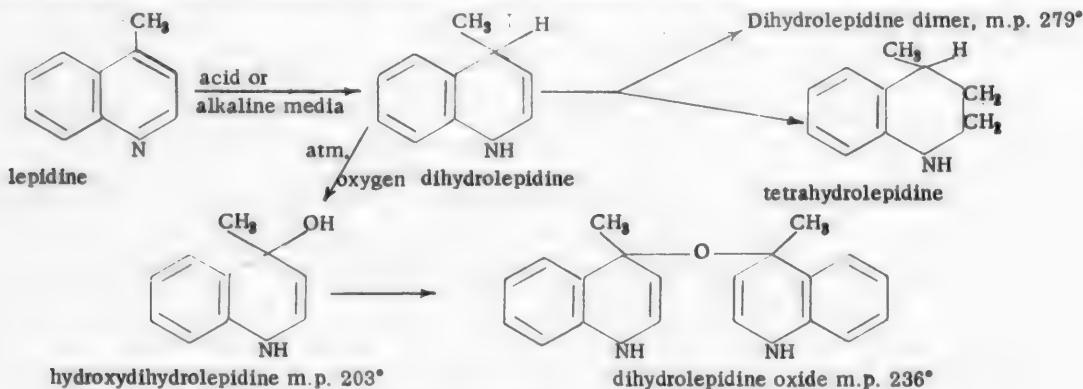
EXPERIMENTAL

Performance of the electrolytic reduction of lepidine in an alkaline medium. We used 1 ml lepidine (1.08 g) per stage of electrolytic reduction. This quantity of lepidine was dissolved in an electrote prepared from 25 ml 18% potassium hydroxide solution and 25 ml 96° ethyl alcohol. The prepared transparent solution was used as a cathode liquid, mercury was the cathode. As an anode region we used a cylindrical glass vessel separated from the cathode region by two layers of cellophane. An 18% solution of potassium hydroxide (20 ml) was poured into the inside of the vessel. A platinum anode was used. Electrolysis was continued for 45 minutes. The current density was 26.6 A/dm^2 at a voltage of 9-11 V. The temperature during electrolysis was held at level not higher than 19° by cooling.

Separation of reaction products. 10.8 g lepidine was reduced under the given conditions in ten portions. At the end of the electrolysis, the cathode liquid (which was very turbid with drops of yellow oily product) was

placed in a separatory funnel and diluted to 100 ml with water used for washing the electrolyzer. An ether extract, which gradually changed color in air from light yellow dark red, was made of the cathode liquid. All the ether extracts were combined together and were permitted to stand in an open vessel in the air for a 48 hour period. During evaporation of ether from the extract, the formation of a crystalline product was observed. When all of the ether had evaporated, the crystalline product was filtered; the yield of this was 1.8 g (16.4%), it was recrystallized several times from boiling toluene; m.p. 279°. Careful study of the properties of this material, together with the data of its ultimate analysis, showed that it was the dimer of dihydrolepidine.

The filtrate, after separation of the dimer of dihydrolepidine, was steam distilled for separation of unreacted lepidine and tetrahydrolepidine. Distillation was continued until the distillate no longer developed a red color with a sulfuric acid solution of potassium dichromate (test for tetrahydrolepidine). The distillate contained an oily product, which was extracted by ether. The ether extract was dried over anhydrous sodium sulfate, and after evaporation of the ether we obtained a yellow oil which was a mixture of unreacted lepidine and tetrahydrolepidine. 4.6 g of this mixture was obtained (42.6%).

After lepidine and tetrahydrolepidine were distilled with steam, a tarry dark brown material was left in the distillation flask; it was filtered from the liquid and on cooling solidified as a solid brittle mass, weight 3.9 g (37%). The filtrate was a light yellow liquid. The tarry product was crushed and worked up in ether. The ether dissolved the tarry material; the undissolved crystalline residue was filtered and dried; dark grey color, weight 0.6 g (5.2%). After repeated recrystallization from toluene we obtained a crystalline product with m.p. 236°.

13.680 mg substance: 39.490 mg CO_2; 8.215 mg H_2O. 11.970 mg substance: 34.512 mg CO_2; 7.273 mg H_2O. 15 540 mg substance: 1.273 ml N_2 (26°, 743 mm). 13.700 mg substance: 1.145 ml N_2, (26.5°, 744 mm). 0.0073 g substance; 0.0854 g camphor: Δt 11.6°. 0.0049 g substance; 0.0678 g camphor: Δt 9.7°. Found %: C 78.79, 78.70; H 6.72, 6.80; N 9.18, 9.32; M 294.7, 298.0 $(C_{10}H_{10}N)_2O$. Calculated %: C 78.91; H 6.61; N 9.20; M 304.4.

Analysis of the picrate. 3.446 mg substance: 0.400 ml N_2 (19°, 742.4 mm). 4.299 mg substance: 0.500 ml N_2 (21°, 742.6 mm). Found %: N 13.25, 13.19. $(C_{10}H_{10}N)_2O \cdot C_6H_2(OH)(NO_2)_3$. Calculated %: N 13.12.

It follows from the above that the material obtained was dihydrolepidine oxide.

From the filtrate obtained after separating the tarry product from the distillation flask, we separated by cooling a yellow colored crystalline substance which weighed 0.62 g (5%) after drying. After repeated recrystallization from boiling toluene a crystalline product with m.p. 203° was obtained.

TABLE 1

Quantity of starting material per 50 ml electrolyte (grams)	Temperature	Current density (Amperes/ Sq. dm.)	Dihydrolepidine yield, based on material (% of theoretical)
3.24	19°	8.8	5.58
3.24	19	17.7	6.16
3.24	19	26.6	6.34
3.24	19	35.4	11.71
3.24	19	42.5	7.54

3.559 mg substance: 9.735 mg CO_2; 2.241 mg H_2O. 3.982 mg substance: 10.900 mg CO_2; 2.530 mg H_2O. 17.020 mg substance: 1.340 ml N_2 (28.5°, 739 mm). 15.800 mg substance: 1.230 ml N_2 (22°, 741 mm). 0.0063 g substance; 0.0692 g camphor: Δt 22.8°. 0.0036 g substance; 0.0720 g camphor: Δt 12.9°. Found %: C 74.66, 74.72; H 7.04, 7.11; N 8.66, 8.84; M 159.7, 155.4. $C_{10}H_{11}ON$. Calculated %: C 74.51; H 6.88, N 8.69; M 161.2.

It follows from the above that the product obtained was hydroxydihydrolepidine. This is also indicated by analysis of the picrate.

4.614 mg substance: 0.593 ml N_2 (25°, 735 mm). 4.350 mg substance: 0.555 ml N_2 (26°, 734 mm). Found %: N 14.22, 14.44. $C_{10}H_{11}ON \cdot C_6H_2(OH)(NO_2)_3$. Calculated %: N 14.35.

In the tables below are given the yields of products of reduction of lepidine (dihydrolepidine dimer, dihydrolepidine oxide, and hydroxydihydrolepidine), recalculated to dihydrolepidine, in relation to the different conditions of electrolysis. In each case the average of 3-5 experiments is given.

Effect of current density on yield of dihydrolepidine. (length of electrolysis 23 minutes, quiescent mercury). The test results are given in Table 1.

It follows from the results obtained that the yield of dihydrolepidine increases with increase in current

density to an optimum value at 35.4 A/dm^2; with furth... increase in current density the yield of dihydrolepidine falls and that of tetrahydrolepidine increases.

Effect of temperature on yield of dihydrolepidine. (length of electrolysis 45 minutes, 3.24 g lepidine in 50 ml electrolyte, current density 35.4 A/dm^2).

The test results are given in Table 2.

Increase in temperature significantly decreases the yield of dihydrolepidine; at higher temperatures the reduction of lepidine leads to tetrahydrolepidine.

Effect of length of electrolysis on dihydrolepidine yield. (3.24 g lepidine in 50 ml electrolyte, current density 35.4 A/dm^2, temperature 19°). Test results are given in Table 3.

TABLE 2

Tempera-ture	Dihydrolepidine yield, based on material (% of theoretical)
19°	12.01
35	6.18
62	3.86

With increase in the length of electrolysis the dihydrolepidine yield, based on material, increases.

Effect of concentration of starting materials on dihydrolepidine yield. (Length of electrolysis 23 minutes, current density 26.6 A/dm^2, temperature 19°). The test results are given in Table 4.

With increasing lepidine concentration in the electrolyte, the yield of dihydrolepidine based on current increases.

Effect of manner (velocity) of mercury renewal on dihydrolepidine yield. The test results are given in Table 5.

Change in manner (velocity) of mercury renewal significantly increases dihydrolepidine yield.

TABLE 3

Length of electrolysis (min.)	Dihydrolepidine yield	
	Based on material (% of theoretical)	Based on current, (%)
10	6.42	11.8
23	11.71	8.72
45	12.01	4.87
90	13.44	1.49
180	17.60	1.79

TABLE 4

Quantity of lepidine (g per 50 ml electrolyte)	Dihydro-lepidine yield, based on current(%)
0.54	3.51
1.08	3.84
1.52	5.33
3.24	6.39
6.48	6.76

TABLE 5

Cathode	Dihydrolepidine yield, based on material (% of theoretical)		
	Length of electrolysis, 45 minutes, current density 35.4 A/dm^2 temp. 16°	Length of electrolysis 45 minutes, current density 26.6 A/dm^2, temp. 18°	
		1.08 g lepidine taken per 50 ml electrolyte	1.08 g lepidine taken per 100 ml electrolyte
Unrenewed mercury cathode	7.21	12.69	24.01
Renewed mercury cathode	11.57	26.56	24.14
Undulating mercury cathode	14.75	0	25.93

SUMMARY

1. It has been shown by our studies that electrolytic reduction of lepidine in alkaline medium leads to formation of dihydrolepidine in the form of its monomer $C_{10}H_{11}N$ which is retained in solution, and that on steam distillation it may be obtained in a mixture with tetrahydrolepidine $C_{10}H_{13}N$ together with unreduced lepidine $C_{10}H_9N$.

2. Dihydrolepidine monomer, which exists in the cathode liquid mixed with tetrahydrolepidine and lepidine, gave at low temperature the dimer of dihydrolepidine, and under action of atmospheric oxygen was oxidized to form two crystalline products: dihydrolepidine oxide $(C_{10}H_{10}N)_2O$ and hydroxydihydrolepidine $C_{10}H_{11}ON$, to which we ascribe the formula of γ-hydroxydihydrolepidine.

LITERATURE CITED

[1] Williams, Chem. News, 37, 85 (1878). [2] V. V. Levchenko and A. A Zats, J. Gen. Chem., 22, 1253 (1952). * [3] V. V. Levchenko, J. Gen. Chem., 18, 1245 (1948). [4] V. V. Levchenko and K. V. Meleshko, J. Gen. Chem., 20, 831 (1950).**[5] Knorr and Klotz, Ber., 19, 3301 (1886).

* See Consultants Bureau translation page 1301.

** See Consultants Bureau translation page 867.

CHEMICAL REDUCTION OF LEPIDINE

A. A. Zats and V. V. Levchenko

Methods for chemical reduction of quinoline and ethylpyridine by boiling with tin and hydrochloric acid and also by treatment with sodium in alcoholic media, were first developed by Vyshnegradsky [1,2]. These methods have not lost their value to the present time and find wide application for reduction of these and other materials. Knorr and Klotz [3], who performed the chemical reduction of lepidine in acid medium by boiling with tin in hydrochloric acid, obtained tetrahydrolepidine. Metallic sodium in an alcohol solution, according to the findings of Mikhailov [4], readily reduced lepidine to tetrahydrolepidine. Williams [5], by action on lepidine of sodium amalgam containing 10% sodium, obtained a yellow oil which when boiled with nitric acid was converted into a crystalline product with a red color whose composition was $C_{10}H_{13}N_2 \cdot HNO_3$; Williams called this material lepidine nitrate.

The purpose of the present investigation was the determination of similarities or differences between chemical reduction of lepidine and its electrolytic reduction, as a result of which we [6,7] had obtained products not previously described in the literature: dihydrolepidine dimer, dihydrolepidine oxide, and γ-hydroxydihydrolepidine.

By chemical reduction of lepidine by the method of Vyshnegradsky using sodium in alcoholic medium, we obtained tetrahydrolepidine. By chemical reduction of lepidine using sodium or potassium amalgam we separated exactly the same products as in electrolytic reduction of lepidine in alkaline medium. By performing the chemical reduction of lepidine by boiling it with tin in hydrochloric acid, we were able to prepare, in addition to tetrahydrolepidine, a crystalline product which appeared to be another isomer of dihydrolepidine, other than the one obtained by us on electrolytic reduction of lepidine in acid or alkaline medium. The yield of raw product was about 1 %. After recrystallization from ligroin we obtained a crystalline white material; small rods, m.p. 187°.

Properties of the product obtained having an m.p. of 187°. The material was insoluble in alkali, readily soluble in hydrochloric acid; on neutralization with alkali it separated unchanged. It was readily soluble in toluene and chloroform when cold; in ligroin and alcohol it was slightly soluble cold and readily soluble on heating. It could be easily purified by recrystallization from the two latter solvents. Like tetrahydrolepidine, it gave an intense color with a solution of potassium dichromate in sulfuric acid. Ultimate analysis gave its elemental composition, which corresponds to the formula $C_{10}H_{11}N$; determination of its molecular weight (by Rast, and by cryoscopic method) showed it to be a dimer of dihydrolepidine $(C_{10}H_{11}N)_2$. This dimer differs sharply from the dimer of dihydrolepidine obtained by us on electrolytic reduction of lepidine in acid medium. A mixture test of both dimers gave significant depression in determination of the melting point.

EXPERIMENTAL

a) Reduction of lepidine by metallic sodium in an alcohol solution. 1 ml (1.08 g) lepidine was dissolved in 10 ml ethyl alcohol, and the solution brought to a boil on a water bath. Metallic sodium, in small pieces, was added to the boiling solution until reaction with alcohol ceased. The solution thickened considerably; on dilution with water no change took place; the solution had a strong alkaline reaction; tests for presence of tetrahydrolepidine with a solution of potassium dichromate in sulfuric acid gave an intense coloration. The solution was extracted with ether, and the extract allowed to stand for evaporation of the ether. The ether extract was barely yellowish in color; the oily material remaining after the ether was evaporated was steam distilled. The presence of tetrahydrolepidine was demonstrated in the products of distillation; the distillate was extracted with ether, and the extract dried over anhydrous sodium sulfate. After evaporation of the ether on a water bath we obtained 0.85 g tetrahydrolepidine, which was identified by its benzoyl derivative. A small amount of yellow colored tarry material formed in the distillation flask. The dry weight of this tar was 0.13 g. The tarry product was readily soluble in ether and alcohol, attempts to separate some crystalline material from the tar gave negative results. We were also unable to obtain any product from the liquid which remained in the distillation flask. Thus, reduction of lepidine by the Vyshnegradsky procedure gave tetrahydrolepidine.

b) Reduction of lepidine by potassium and sodium amalgams. For the chemical reduction, we took 3 ml (3.24 g) lepidine and dissolved it in 50 ml of a mixture of 25 ml alcohol and 25 ml 18% potassium hydroxide solution. The prepared solution was poured onto a 1.5% potassium amalgam, 50 ml volume; reduction continued for 45 minutes with energetic stirring. The temperature was held at a level below 18° by cooling. After a lapse of 45 minutes the mercury was separated from the liquid, which contained droplets of a yellow oily product, using a separatory funnel. The solution was extracted by ether and the extract worked up in the same manner as had been used in the electrolytic reduction of lepidine in alkaline medium [7]. As a result we obtained the following quantities of products: dihydrolepidine dimer 0.22 g (6.7%), dihydrolepidine oxide 0.41 g (11.8%), hydroxydihydrolepidine 0.14 g (4.2%), tarry product from the distillation flask 1.39 g (43%), and a mixture of lepidine and tetrahydrolepidine 1.1 g (33.9%). The total yield of the first three products, recalculated to dihydrolepidine, amounted to 22.4% by weight of the theoretical. Increase in length of reduction to 3.5 hours increased the yield of products, recalculated to dihydrolepidine, to 32.7%. Reduction of lepidine by sodium amalgam took place in a similar manner. Performing these experiments on chemical reduction of lepidine by potassium and sodium amalgam, show that there was no difference between chemical reduction and electrolytic reduction of lepidine in alkaline medium using a quiescent mercury cathode.

c) Chemical reduction of lepidine in acid medium. 3 ml (3.24 g) lepidine was dissolved in 50 ml concentrated hydrochloric acid; 15 g granular tin was added to the prepared solution, and the entire mixture boiled on a sand bath for 8 hours in a round-bottom flask fitted with a reflux condenser. At the end of the stated time, the hot solution was decanted from the very small quantity of unreacted tin which remained. On cooling the solution, white and yellow colored crystals separated, which were evidently a mixture of double tin salts of lepidine hydrochloride and the products of its reduction. The crystals which separated were suction filtered and washed with weakly acidified ice water. The double salts were treated with a concentrated solution of potassium hydroxide; the dark brown colored solution thus obtained was steam distilled. The first portions of the distillate gave an intense color with a solution of potassium dichromate in sulfuric acid (test for tetrahydrolepidine); steam distillation was continued until reaction with potassium dichromate ceased. The distillate was extracted by ether. The ether extract was dried over anhydrous sodium sulfate. The ether was distilled on a water bath, and as a residue we obtained an oily product which was a mixture of unreacted lepidine and tetrahydrolepidine. 2.25 g (69.4%) of this mixture was obtained. The liquid which remained in the distillation flask was filtered. A dirty brown colored residue containing admixed tar was collected on the filter. This residue was dried and worked up in ether — which did not completely dissolve the residue. The undissolved portion was removed by filtration — it appeared to be an inorganic residue. The ether solution after evaporation of the ether yielded a yellow resinous substance (total weight 0.48 g), in which a small amount of crystalline material was found. The resinous material was dissolved in a small quantity of alcohol with warming; the solution obtained had a yellow color. A white crystalline material separated from the alcohol solution on cooling and scratching with a glass rod; the dried product weighed 0.04 g (1%). Recrystallization from alcohol or ligroin gave a crystalline product with an m.p. of 187°.

2.821 mg substance: 8.542 mg CO_2; 1.950 mg H_2O. 2.806 mg substance: 8.491 mg CO_2; 1.923 mg H_2O. 3.147 mg substance: 0.265 ml N_2 (18.5°, 745 mm). 3.198 mg substance: 0.271 ml N_2 (18.5° 748 mm). 0.0052 g substance; 0.0696 g camphor: Δt 10.5°. 0.0047 g substance; 0.0819 g camphor: Δt 8.25°. 0.0414 g substance: 4.08 g benzene: Δt 0.17°. 0.0704 g substance; 4.08 g benzene: Δt 0.29°. Found %: C 82.65, 82.60; H 7.67, 7.73; N 9.66, 9.77; M 284.6, 278.3, 304.4, 303.5. $(C_{10}H_{11}N)_2$. Calculated %: C 82.71; H 7.64; N 9.65; M 290.4.

From the above given data it follows that the product prepared was a dimer of dihydrolepidine $(C_{10}H_{11}N)_2$.

SUMMARY

1. Performance of the study showed that lepidine, on chemical reduction in acid medium, yields in addition to tetrahydrolepidine a new crystalline product which is not obtained by reduction of lepidine via other methods.

2. It was shown that this product was a heretofore unprepared isomer of dihydrolepidine dimer, which differed from the dimer of dihydrolepidine obtained on electrolytic reduction of lepidine in acid and alkaline media.

3. It has been shown that there is no difference in principle between chemical reduction of lepidine using potassium or sodium amalgam and the electrolytic reduction of lepidine in alkaline medium on a mercury cathode.

LITERATURE CITED

[1] A. N. Vyshnegradsky, J. Russ. Chem. Soc., 12, II, 16 (1880)

[2] A. N. Vyshnegradsky, Ber., 13, 2400 (1880).

[3] Knorr and Klotz, Ber., 19, 3301 (1886).

[4] G. I. Mikhailov, collected works of the I.R.E.A.* , 18, 39 (1941).

[5] Williams, Chem. News, 37, 85 (1878).

[6] V. V. Levchenko and A. A. Zats, J. Gen. Chem., 22, 1253 (1952).**

[7] V. V. Levchenko and A. A. Zats, J. Gen. Chem. 22, 2071***(1952).

Received June 9, 1951   Moscow Institute of Stomatological Medicine

* Institute of Chemical Reagents.
** See Consultants Bureau English Translation, p. 130D.
*** See Consultants Bureau English Translation, p. 2125.

BLANK PAGE